Electronic Supporting Information for

Acetic Acid-Promoted Cascade *N*-Acyliminium ion/*aza*-Prins Cyclization: Stereoselective Synthesis of Functionalized Fused Tricyclic Piperidines

Rajiv T. Sawant[a], Marc Y. Stevens[a] and Luke R. Odell*[a]

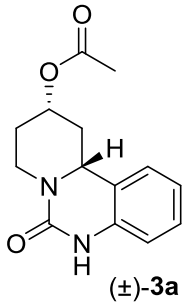
[a]Organic Pharmaceutical Chemistry, Department of Medicinal Chemistry, Uppsala Biomedical Center, Uppsala University, P.O. Box 574, SE-751 23 Uppsala, Sweden

Contents

General Information

All reagents were purchased at the highest commercial quality and used without further purification. Yields refer to isolated, homogenous and spectroscopically pure material, unless otherwise stated. Crude reaction mixtures were purified by silica gel chromatography (E. Merck silica gel, particle size 0.043–0.063 mm) and thin layer chromatography was carried out using E. Merck silica plates (60F-254) with UV light (254 nm) as the visualization agent. Microwave reactions were carried out in an Initiator single-mode reactor producing controlled radiation at 2450 MHz, and temperature was monitored via the built-in online IR sensor. ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C{^{1}H} NMR spectra at 100 MHz. The chemical shifts for ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were referenced to tetramethylsilane *via* residual solvent signals (^{1}H, $CDCl_3$ at 7.26 ppm, CD_3OD at 3.31 ppm; ^{13}C, $CDCl_3$ at 77.16 ppm, CD_3OD at 49.0 ppm). LC/MS was performed on an instrument equipped with a C18 column (50 × 3.0 mm, particle size 2.6 µm, pore size 100 Å). Accurate mass values were determined using a mass spectrometer equipped with an electrospray ion source and time-of-flight detector. Electrophilic precursors **1a–1m** were prepared following the literature procedure.[1,2]

General procedure for cascade aza-Prins cyclisation, exemplified by the preparation of (±)-6-Oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (3a)



(±)-**3a**

Chemical Formula: $C_{14}H_{16}N_2O_3$
Exact Mass: 260.1161

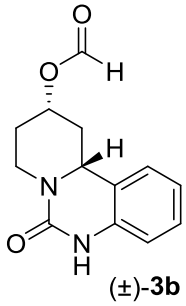
A sealed 0.5–2 mL Pyrex process vial charged with aldehyde **1a** (40 mg, 223 µmol), amine **2a** (20 mg, 281 µmol) and acetic acid (1 mL) was subjected to microwave irradiation at 140 °C for 20 min. The reaction mixture was cooled to room temperature, diluted with 2 mL ethyl acetate. The volatiles were concentrated in vacuo and the residue was purified by silica gel chromatography (55% EtOAc in *n*-pentane) to yield the title compound as a white solid (49 mg, 189 µmol, 86%, 99/1 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.58–1.69 (m, 1H), 1.99–2.03 (m, 1H), 2.04 (s, 4H), 2.27 (ddt, *J* = 12.4, 4.6, 2.3, 2.3 Hz, 1H), 2.73 (ddd, *J* = 13.8, 12.9, 2.6 Hz, 1H), 4.55 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.69 (ddd, *J* = 13.8, 4.6, 2.4 Hz, 1H), 4.90–5.26 (m, 1H), 6.61–6.76 (m, 1H), 6.91–6.98 (m, 1H), 7.00–7.07 (m, 1H), 7.11–7.20 (m, 1H), 7.88 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.4, 30.6, 39.7, 41.8, 56.6, 71.1, 114.0, 120.0, 122.3, 125.6, 128.7, 135.7, 152.8, 170.5.

HRMS (ESI) calc'd for $C_{16}H_{20}N_3O_3$ *m/z* 302.1505, found *m/z* 302.1508 (MeCN + H^+ adduct).

(±)-6-Oxo-5,8,9,10,11,11a-hexahydro-6H-pyrido[1,2-c]quinazolin-10-yl)formate (3b)



(±)-**3b**

Chemical Formula: $C_{13}H_{14}N_2O_3$
Exact Mass: 246.1004

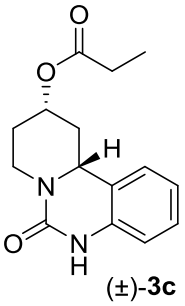
Prepared following the general procedure, using formic acid (1 mL) instead of AcOH. Starting from aldehyde **1a** (40 mg, 223 µmol) and amine **2a** (20 mg, 281 µmol), the title compound was obtained after silica gel chromatography (55% EtOAc in *n*-pentane) as a white solid (20 mg, 83 µmol, 36%, 99/1 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.63–1.74 (m, 1H), 2.00 – 2.10 (m, 1H), 2.21–2.35 (m, 1H), 2.74 (td, *J* = 13.4, 13.4, 2.6 Hz, 1H), 4.56 (dd, *J* = 11.9, 2.6 Hz, 1H), 4.72 (ddd, *J* = 13.9, 4.7, 2.4 Hz, 1H), 5.12–5.22 (m, 1H), 6.72 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.88–7.00 (m, 1H), 7.00–7.07 (m, 1H), 7.11–7.23 (m, 1H), 8.03 (s, 1H), 8.27 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 30.5, 39.5, 41.7, 56.5, 70.9, 114.2, 119.7, 122.3, 125.5, 128.8, 135.8, 153.0, 160.4.

HRMS (ESI) calc'd for $C_{13}H_{15}N_2O_3$ *m/z* 247.1083, found *m/z* 247.1092.

(±)-6-Oxo-5,8,9,10,11,11a-hexahydro-6H-pyrido[1,2-c]quinazolin-10-yl propionate (3c)



(±)-**3c**

Chemical Formula: $C_{15}H_{18}N_2O_3$
Exact Mass: 274.1317

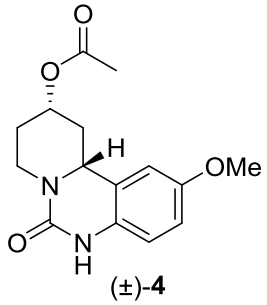
Prepared following the general procedure, using propionic acid (1 mL) instead of AcOH. Starting from aldehyde **1a** (40 mg, 223 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (30–55% EtOAc in *n*-pentane) as a white solid (31 mg, 113 µmol, 51%, 97/3 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.12 (t, *J* = 7.6, 7.6 Hz, 3H), 1.55–1.67 (m, 1H), 1.67–1.75 (m, 1H), 1.97–2.07 (m, 1H), 2.23–2.29 (m, 2H), 2.29–2.34 (m, 1H), 2.64–2.80 (m, 1H), 4.54 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.69 (ddd, *J* = 13.8, 4.7, 2.4 Hz, 1H), 5.03 (ddd, *J* = 11.3, 6.7, 4.6 Hz, 1H), 6.70–6.77 (m, 1H), 6.89–6.95 (m, 1H), 6.99–7.04 (m, 1H), 7.13–7.19 (m, 1H), 8.71 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 27.8, 30.5, 39.6, 41.6, 56.4, 70.7, 114.0, 119.8, 122.0, 125.3, 128.5, 135.8, 153.1, 173.8.

HRMS (ESI) calc'd for $C_{17}H_{22}N_3O_3$ *m/z* 316.1661, found *m/z* 316.1675 (MeCN + H^+ adduct).

(±)-2-Methoxy-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (4)



(±)-**4**

Chemical Formula: $C_{15}H_{18}N_2O_4$

Exact Mass: 290.1267

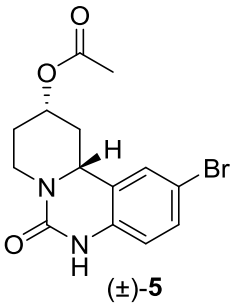
Prepared following the general procedure, starting from aldehyde **1b** (40 mg, 191 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (70% EtOAc in *n*-pentane) as a white solid (48 mg, 164 µmol, 86%, 96/4 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.59–1.76 (m, 2H), 1.97–2.04 (m, 1H), 2.04 (s, 3H), 2.23–2.34 (m, 1H), 2.71 (ddd, *J* = 13.8, 12.9, 2.6 Hz, 1H), 3.75 (s, 3H), 4.50 (dd, *J* = 12.0, 2.5 Hz, 1H), 4.68 (ddd, *J* = 13.8, 4.6, 2.4 Hz, 1H), 5.01 (tt, *J* = 11.3, 11.3, 4.6, 4.6 Hz, 1H), 6.58 (d, *J* = 2.7 Hz, 1H), 6.63 (d, *J* = 8.6 Hz, 1H), 6.73 (dd, *J* = 8.6, 2.7 Hz, 1H), 7.80 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.4, 30.5, 39.4, 41.8, 55.8, 56.8, 71.1, 110.9, 114.4, 115.0, 120.9, 129.3, 152.9, 155.2, 170.5.

HRMS (ESI) calc'd for $C_{15}H_{19}N_2O_4$ *m/z* 291.1345, found *m/z* 291.1343.

(±)-2-Bromo-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (5)



(±)-**5**

Chemical Formula: $C_{14}H_{15}BrN_2O_3$

Exact Mass: 338.0266

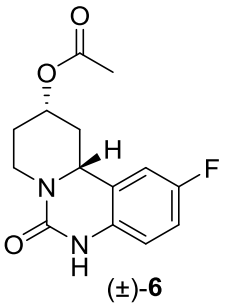
Prepared following the general procedure, starting from aldehyde **1c** (40 mg, 155 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (45% EtOAc in *n*-pentane) as a white solid (45 mg, 132 µmol, 85%, 95/5 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.56–1.78 (m, 2H), 2.05 (s, 3H), 2.27 (ddt, *J* = 12.3, 4.6, 2.3, 2.3 Hz, 1H), 2.72 (ddd, *J* = 13.8, 13.0, 2.6 Hz, 1H), 4.52 (dd, *J* = 12.3, 2.6 Hz, 1H), 4.67 (ddd, *J* = 13.8, 4.6, 2.4 Hz, 1H), 5.00 (tt, *J* = 11.3, 11.3, 4.6, 4.6 Hz, 1H), 6.61 (d, *J* = 8.5 Hz, 1H), 7.16 (d, *J* = 2.1 Hz, 1H), 7.24–7.28 (m, 1H), 8.33 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.3, 30.5, 39.6, 41.8, 56.1, 70.8, 114.3, 115.7, 121.9, 128.5, 131.6, 135.0, 152.6, 170.5.

HRMS (ESI) calc'd for $C_{16}H_{19}BrN_3O_3$ *m/z* 380.0160, found *m/z* 380.0628 (MeCN + H^+) adduct.

(±)-2-Fluoro-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (6)



(±)-**6**

Chemical Formula: $C_{14}H_{15}FN_2O_3$

Exact Mass: 278.1067

Prepared following the general procedure, starting from aldehyde **1d** (40 mg, 203 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (53% EtOAc in *n*-pentane) as a white solid (46 mg, 165 µmol, 81%, 96/4 *cis*/*trans* ratio).

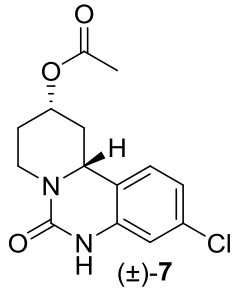
^{1}H NMR (400 MHz; $CDCl_3$) δ 1.57–1.78 (m, 2H), 2.00–2.04 (m, 1H), 2.05 (s, 3H), 2.26 (ddt, *J* = 12.4, 4.6, 2.3, 2.3 Hz, 1H), 2.72 (ddd, *J* = 13.8, 12.9, 2.6 Hz, 1H), 4.52 (dd, *J* = 11.9, 2.6

Hz, 1H), 4.68 (ddd, *J* = 13.9, 4.6, 2.4 Hz, 1H), 4.85–5.21 (m, 1H), 6.67 (dd, *J* = 8.7, 4.6 Hz, 1H), 6.76 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.83–6.98 (m, 1H), 8.31 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.7, 30.8, 39.7, 42.1, 56.7 (d, $^4J_{CF}$ = 1.9 Hz), 71.2, 112.7 (d, $^2J_{CF}$ = 24.0 Hz), 115.57 (d, $^3J_{CF}$ = 7.8 Hz), 115.87 (d, $^2J_{CF}$ = 22.9 Hz), 121.6 (d, $^3J_{CF}$ = 7.3 Hz), 132.4 (d, $^4J_{CF}$ = 2.3 Hz), 153.2, 158.6 (d, $^1J_{CF}$ = 240.7 Hz), 170.8.

HRMS (ESI) calc'd for $C_{16}H_{19}FN_3O_3$ *m/z* 320.1410, found *m/z* 320.1414 (MeCN + H^+ adduct).

(±)-3-Chloro-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (7)



(±)-**7**

Chemical Formula: $C_{14}H_{15}ClN_2O_3$
Exact Mass: 294.0771

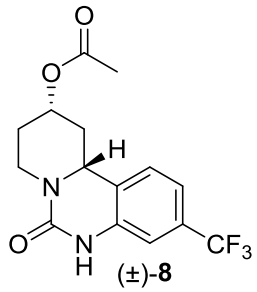
Prepared following the general procedure, starting from aldehyde **1e** (40 mg, 203 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (45% EtOAc in *n*-pentane) as a white solid (45 mg, 155 µmol, 83%, 94/6 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.56–1.78 (m, 3H), 2.05 (s, 3H), 2.21–2.31 (m, 1H), 2.68–2.80 (m, 1H), 4.52 (dd, *J* = 11.9, 2.6 Hz, 1H), 4.69 (ddd, *J* = 13.7, 4.7, 2.4 Hz, 1H), 4.96–5.06 (m, 1H), 6.73 (d, *J* = 1.9 Hz, 1H), 6.90 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 8.36 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.2, 30.4, 39.5, 41.7, 56.0, 70.7, 113.8, 118.3, 122.2, 126.6, 134.1, 136.8, 152.3, 170.3.

HRMS (ESI) calc'd for $C_{16}H_{19}ClN_3O_3$ *m/z* 336.1115, found *m/z* 336.1128 (MeCN + H^+ adduct).

(±)-6-Oxo-3-(trifluoromethyl)-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (8)



(±)-**8**

Chemical Formula: $C_{15}H_{15}F_3N_2O_3$
Exact Mass: 328.1035

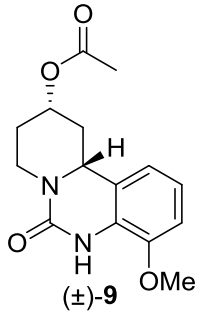
Prepared following the general procedure, starting from aldehyde **1f** (40 mg, 161 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (45% EtOAc in *n*-pentane) as a white solid (45 mg, 136 µmol, 84%, 93/7 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.61–1.80 (m, 3H), 2.05 (s, 3H), 2.25–2.35 (m, 1H), 2.68–2.84 (m, 1H), 4.60 (dd, *J* = 12.1, 2.5 Hz, 1H), 4.71 (ddd, *J* = 13.9, 4.6, 2.4 Hz, 1H), 5.04 (tt, *J* = 11.3, 11.3, 4.6, 4.6 Hz, 1H), 6.95–6.98 (m, 1H), 7.12–7.16 (m, 1H), 7.17–7.21 (m, 1H), 8.75 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.3, 30.5, 39.5, 41.9, 56.4, 70.8, 111.0 (q, $^3J_{CF}$ = 3.7 Hz), 118.9 (q, $^3J_{CF}$ = 3.9 Hz), 123.4 (q, $^4J_{CF}$ = 1.5 Hz), 123.7 (q, $^1J_{CF}$ = 270.2 Hz), 126.2, 131.3 (q, $^2J_{CF}$ = 32.5 Hz), 136.5, 152.7, 170.5.

HRMS (ESI) calc'd for $C_{17}H_{19}F_3N_3O_3$ *m/z* 370.1379, found *m/z* 370.1378.

(±)-4-Methoxy-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (9)



(±)-**9**

Chemical Formula: $C_{15}H_{18}N_2O_4$
Exact Mass: 290.1267

Prepared following the general procedure, starting from aldehyde **1g** (40 mg, 191 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (60% EtOAc in *n*-pentane) as a white solid (38 mg, 130 µmol, 68%, 97/3 *cis*/*trans* ratio). A single crystal was prepared for X-ray diffraction studies by recrystallization from THF/pentane. CCDC 1519982 contains the supplementary crystallographic data for this

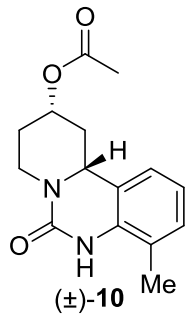
paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.57–1.76 (m, 2H), 1.98–2.04 (m, 1H), 2.04 (s, 3H), 2.22–2.32 (m, 1H), 2.71 (ddd, *J* = 13.8, 12.9, 2.6 Hz, 1H), 3.85 (s, 3H), 4.55 (dd, *J* = 12.0, 2.5 Hz, 1H), 4.68 (ddd, *J* = 13.8, 4.7, 2.4 Hz, 1H), 5.00 (tt, *J* = 11.3, 11.3, 4.6, 4.6 Hz, 1H), 6.63–6.67 (m, 1H), 6.71–6.78 (m, 1H), 6.87–6.92 (m, 1H), 6.93–6.98 (m, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.4, 30.6, 39.5, 41.8, 55.9, 56.7, 71.1, 109.5, 117.3, 120.2, 122.0, 125.3, 145.0, 151.9, 170.5.

HRMS (ESI) calc'd for $C_{15}H_{19}N_2O_4$ *m/z* 291.1345, found *m/z* 291.1359.

(±)-4-Methyl-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (10)



(±)-**10**

Chemical Formula: $C_{15}H_{18}N_2O_3$
Exact Mass: 274.1317

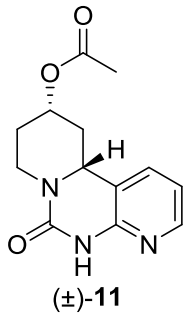
Prepared following the general procedure, starting from aldehyde **1h** (40 mg, 207 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (50% EtOAc in *n*-pentane) as a white solid (43 mg, 155 µmol, 75%, 97/3 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.58–1.78 (m, 2H), 1.98–2.02 (m, 1H), 2.04 (s, 3H), 2.19 (s, 3H), 2.21–2.29 (m, 1H), 2.66–2.80 (m, 1H), 4.53 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.66 (ddd, *J* = 13.8, 4.7, 2.4 Hz, 1H), 5.02 (ddd, *J* = 11.3, 6.7, 4.6 Hz, 1H), 6.76–6.92 (m, 3H), 6.98–7.06 (m, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 16.6, 21.2, 30.4, 39.6, 41.7, 56.5, 70.9, 119.6, 121.2, 121.9, 123.3, 129.8, 133.7, 152.3, 170.4.

HRMS (ESI) calc'd for $C_{17}H_{22}N_3O_3$ *m/z* 316.1661, found *m/z* 316.1675 (MeCN + H^+ adduct).

(±)-6-Oxo-5,8,9,10,11,11a-hexahydro-6*H*-dipyrido[1,2-*c*:3',2'-*e*]pyrimidin-10-yl acetate (11)



(±)-**11**

Chemical Formula: $C_{13}H_{15}N_3O_3$
Exact Mass: 261.1113

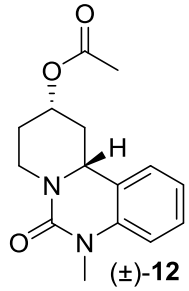
Prepared following the general procedure, starting from aldehyde **1i** (40 mg, 222 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (50% EtOAc in *n*-pentane) as a white solid (36 mg, 137 µmol, 62%, 92/8 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.57–1.77 (m, 2H), 2.00–2.03 (m, 1H), 2.05 (s, 3H), 2.27 (ddt, *J* = 12.3, 4.6, 2.4, 2.4 Hz, 1H), 2.73 (ddd, *J* = 13.9, 13.0, 2.6 Hz, 1H), 4.56 (dd, *J* = 12.0, 2.7 Hz, 1H), 4.70 (ddd, *J* = 14.0, 4.7, 2.4 Hz, 1H), 5.01 (tt, *J* = 11.3, 11.3, 4.6, 4.6 Hz, 1H), 6.91 (dd, *J* = 7.5, 5.0 Hz, 1H), 7.37 (ddd, *J* = 7.5, 1.7, 0.8 Hz, 1H), 8.23 (ddd, *J* = 5.0, 1.7, 0.6 Hz, 1H), 8.81 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.2, 30.4, 39.4, 41.4, 55.3, 70.6, 115.4, 117.9, 133.8, 147.8, 148.9, 152.0, 170.3.

HRMS (ESI) calc'd for $C_{13}H_{16}N_3O_3$ *m/z* 262.1192, found *m/z* 262.1210.

(±)-5-Methyl-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (12)



(±)-**12**

Chemical Formula: $C_{15}H_{18}N_2O_3$
Exact Mass: 274.1317

Prepared following the general procedure, starting from aldehyde **1j** (40 mg, 207 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (30% EtOAc in *n*-pentane) as a white solid (44 mg, 160 µmol, 77%, 98/2 *cis*/*trans* ratio).

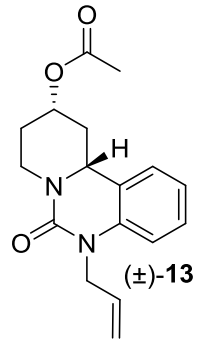
^{1}H NMR (400 MHz; $CDCl_3$) δ 1.58–1.73 (m, 2H), 1.96–2.02 (m, 1H), 2.03 (s, 3H), 2.21 (ddt, *J* = 12.3, 4.5, 2.4, 2.4 Hz, 1H), 2.74 (ddd, *J* = 13.8, 12.9, 2.6 Hz, 1H), 3.33 (s, 3H), 4.46 (dd, *J*

= 12.0, 2.6 Hz, 1H), 4.64 (ddd, *J* = 13.8, 4.6, 2.4 Hz, 1H), 5.02 (ddd, *J* = 11.4, 6.7, 4.7 Hz, 1H), 6.83 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.98 (td, *J* = 7.4, 7.4, 1.1 Hz, 1H), 7.05 (ddt, *J* = 7.5, 1.7, 0.6, 0.6 Hz, 1H), 7.22–7.32 (m, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.2, 30.0, 30.2, 39.2, 43.1, 55.8, 71.0, 112.9, 121.7, 122.0, 125.5, 128.5, 138.1, 153.3, 170.3.

HRMS (ESI) calc'd for $C_{15}H_{19}N_2O_3$ *m/z* 275.1396, found *m/z* 275.1400.

(±)-5-Allyl-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (13)



Chemical Formula: $C_{17}H_{20}N_2O_3$
Exact Mass: 300.1474

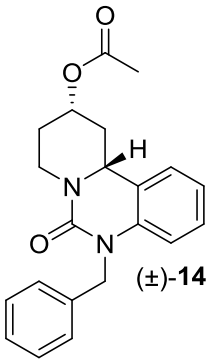
Prepared following the general procedure, starting from aldehyde **1k** (40 mg, 182 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (32% EtOAc in *n*-pentane) as a white solid (45 mg, 150 µmol, 82%, 93/7 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.58–1.75 (m, 2H), 1.96–2.00 (m, 1H), 2.03 (s, 3H), 2.18–2.29 (m, 1H), 2.74 (ddd, *J* = 13.8, 13.0, 2.6 Hz, 1H), 4.35–4.51 (m, 2H), 4.54–4.74 (m, 2H), 5.02 (ddd, *J* = 11.4, 6.7, 4.7 Hz, 1H), 5.13–5.22 (m, 2H), 5.8–5.97 (m, 1H), 6.75–6.84 (m, 1H), 6.93–7.02 (m, 1H), 7.03–7.09 (m, 1H), 7.17–7.24 (m, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.3, 30.3, 39.5, 43.2, 45.3, 56.0, 71.1, 113.9, 116.2, 121.8, 122.1, 125.7, 128.5, 133.1, 137.3, 153.0, 170.5.

HRMS (ESI) calc'd for $C_{17}H_{21}N_2O_3$ *m/z* 301.1552, found *m/z* 301.1549.

(±)-5-Benzyl-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (14)



(±)-**14**

Chemical Formula: $C_{21}H_{22}N_2O_3$
Exact Mass: 350.1630

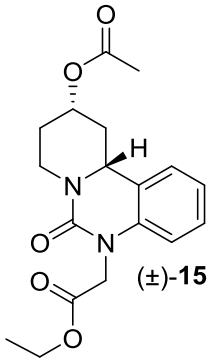
Prepared following the general procedure, starting from aldehyde **1l** (40 mg, 182 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (35% EtOAc in *n*-pentane) as a white liquid (43 mg, 122 µmol, 82%, 93/7 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.64–1.81 (m, 2H), 2.00–2.04 (m, 1H), 2.06 (s, 3H), 2.23–2.32 (m, 1H), 2.65 – 3.38 (m, 1H), 4.54 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.71 (ddd, *J* = 13.8, 4.6, 2.4 Hz, 1H), 4.99–5.14 (m, 2H), 5.17–5.28 (m, 1H), 6.70 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.94 (td, *J* = 7.5, 7.5, 1.0 Hz, 1H), 7.02–7.14 (m, 2H), 7.16–7.28 (m, 3H), 7.27–7.38 (m, 2H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.7, 30.8, 40.1, 43.7, 47.0, 56.5, 71.5, 114.5, 122.1, 122.6, 126.1, 126.7, 127.4, 128.9, 129.1, 137.6, 138.0, 153.8, 170.8.

HRMS (ESI) calc'd for $C_{21}H_{23}N_2O_3$ *m/z* 351.1709, found *m/z* 351.1700.

(±)-Ethyl-2-(10-acetoxy-6-oxo-9,10,11,11a-tetrahydro-6*H*-pyrido[1,2-*c*]quinazolin-5(8*H*)-yl)acetate (15)



(±)-**15**

Chemical Formula: $C_{18}H_{22}N_2O_5$
Exact Mass: 346.1529

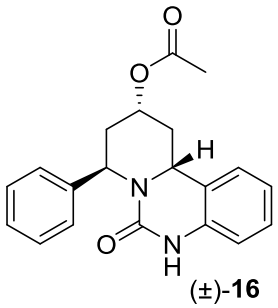
Prepared following the general procedure, starting from aldehyde **1m** (40 mg, 150 µmol) and amine **2a** (21 mg, 295 µmol), the title compound was obtained after silica gel chromatography (35% EtOAc in *n*-pentane) as a yellow liquid (38 mg, 109 µmol, 72%, 96/4 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.26 (t, *J* = 7.1, 7.1 Hz, 3H), 1.60–1.81 (m, 2H), 1.96–2.02 (m, 1H), 2.03 (s, 3H), 2.23 (ddt, *J* = 12.4, 4.5, 2.2, 2.2 Hz, 1H), 2.77 (ddd, *J* = 13.8, 13.0, 2.6 Hz, 1H), 4.14–4.28 (m, 2H), 4.49 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.57–4.68 (m, 1H), 4.59–4.76 (m, 2H), 5.03 (ddd, *J* = 11.3, 6.7, 4.7 Hz, 1H), 6.61 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.99 (td, *J* = 7.5, 7.4, 1.0 Hz, 1H), 7.07 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.21 (ddd, *J* = 8.5, 7.3, 1.6 Hz, 1H).

NMR (100 MHz; $CDCl_3$) δ 14.2, 21.2, 30.2, 39.3, 43.2, 44.4, 56.0, 61.4, 70.9, 112.6, 121.8, 122.4, 125.9, 128.6, 137.0, 152.9, 169.2, 170.4.

HRMS (ESI) calc'd for $C_{18}H_{23}N_2O_5$ *m/z* 347.1607, found *m/z* 347.1606.

(±)-6-Oxo-8-phenyl-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (16)



(±)-**16**

Chemical Formula: $C_{20}H_{20}N_2O_3$

Exact Mass: 336.1474

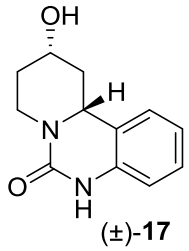
Prepared following the general procedure, starting from aldehyde **1a** (40 mg, 150 µmol) and amine **2b** (150 mg, 1 mmol, prepared following the literature procedure[3]), the title compound was obtained after silica gel chromatography (25% EtOAc in *n*-pentane) as a colorless liquid (40 mg, 119 µmol, 55%, 98/2 *cis*/*trans* ratio).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.85 (td, *J* = 12.2, 12.2, 11.2 Hz, 1H), 1.94–2.05 (m, 1H), 2.07 (s, 3H), 2.14 (ddt, *J* = 12.4, 4.8, 2.3, 2.3 Hz, 1H), 2.83 (ddt, *J* = 13.4, 4.2, 2.0, 2.0 Hz, 1H), 4.47 (dd, *J* = 12.2, 2.6 Hz, 1H), 5.13–5.26 (m, 1H), 6.20 (d, *J* = 5.4 Hz, 1H), 6.68–6.79 (m, 1H), 6.91 (dd, *J* = 4.2, 0.8 Hz, 2H), 7.09–7.22 (m, 1H), 7.26 – 7.33 (m, 1H), 7.38 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.47 (dt, *J* = 8.3, 1.2, 1.2 Hz, 2H), 8.18 (s, 1H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 21.3, 31.3, 40.0, 51.7, 52.1, 67.9, 113.9, 119.8, 122.2, 125.9, 126.7, 127.2, 128.5, 129.0, 135.4, 137.7, 153.4, 170.5.

HRMS (ESI) calc'd for $C_{20}H_{21}N_2O_3$ *m/z* 337.1552, found *m/z* 337.1559.

(±)-10-Hydroxy-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-6-one (17)



(±)-**17**

Chemical Formula: $C_{12}H_{14}N_2O_2$

Exact Mass: 218.1055

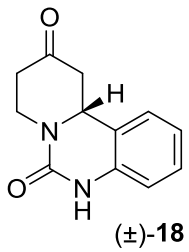
To a stirred solution of **3a** (30 mg, 115 µmol) in methanol (1 mL) at ambient temperature was added K_2CO_3 (34 mg, 246 µmol). The resulting solution was stirred for 17 h, after which it was partitioned between brine (10 mL) and EtOAc (10 mL). The aqueous phase was extracted into EtOAc (2x20 mL), and the combined organics were dried over $MgSO_4$ and concentrated in vacuo. Silica gel chromatography (6% MeOH in DCM) provided the title product as a white solid (22 mg, 100 µmol, 88%). This transformation can also be carried out using NaOH, resulting in a slightly altered diastereomeric *cis/trans* ratio (87:13 vs. 89:11 using K_2CO_3).

^{1}H NMR (400 MHz; $CDCl_3$) δ 1.23–1.61 (m, 2H), 1.87–2.03 (m, 1H), 2.12 (ddd, *J* = 12.4, 4.5, 2.3 Hz, 1H), 2.70 (td, *J* = 13.4, 13.3, 2.6 Hz, 1H), 3.85 (tt, *J* = 11.0, 11.0, 4.5, 4.5 Hz, 1H), 4.45 (ddd, *J* = 13.7, 4.5, 2.4 Hz, 1H), 4.52 (dd, *J* = 11.9, 2.5 Hz, 1H), 6.72 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.92 (td, *J* = 7.5, 7.5, 1.2 Hz, 1H), 7.06–7.16 (m, 2H).

^{13}C NMR (100 MHz; $CDCl_3$) δ 33.7, 41.5, 43.0, 56.5, 68.1, 113.4, 120.6, 121.9, 125.2, 127.9, 135.6, 153.5.

HRMS (ESI) calc'd for $C_{12}H_{15}N_2O_2$ *m/z* 219.1134, found *m/z* 219.1132.

(±)-8,9,11,11a-Tetrahydro-6*H*-pyrido[1,2-*c*]quinazoline-6,10(5*H*)-dione (18)



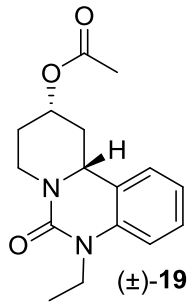
(±)-**18**

Chemical Formula: $C_{12}H_{12}N_2O_2$

Exact Mass: 216.0899

To a stirred suspension of **17** (50 mg, 229 µmol) in DCM (5 mL) at ambient temperature was added DMP (97 mg, 229 µmol). The resulting mixture was stirred at ambient temperature overnight, after which sat. $NaHCO_3$ (10 mL) and $Na_2S_2O_3$ (26 mg) was added. The resulting aqueous phase was extracted into diethyl ether (2x40 mL), after which the combined organics were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (30% EtOAc in hexanes) to yield the title compound as a white solid (35 mg, 164 µmol, 72%). Spectral data were in agreement with literature values. [2]

(±)-5-Ethyl-6-oxo-5,8,9,10,11,11a-hexahydro-6*H*-pyrido[1,2-*c*]quinazolin-10-yl acetate (19)



(±)-**19**

Chemical Formula: $C_{16}H_{20}N_2O_3$
Exact Mass: 288.1474

To a stirred solution of **3a** (30 mg, 115 µmol) in DMF (1 mL) at ambient temperature was added NaH (5 mg, 60% dispersion in paraffin) and EtI (20 mg, 128 µmol). The resulting mixture was stirred for 40 min, after which it was partitioned between brine (10 mL) and EtOAc (10 mL). The aqueous phase was extracted into EtOAc (2x20 mL), and the combined organics were dried over $MgSO_4$ and concentrated in vacuo. Silica gel chromatography (30% EtOAc in *n*-pentane) provided the title product as a yellow solid (25 mg, 87 µmol, 75%, 94/6 *cis*/*trans* ratio).

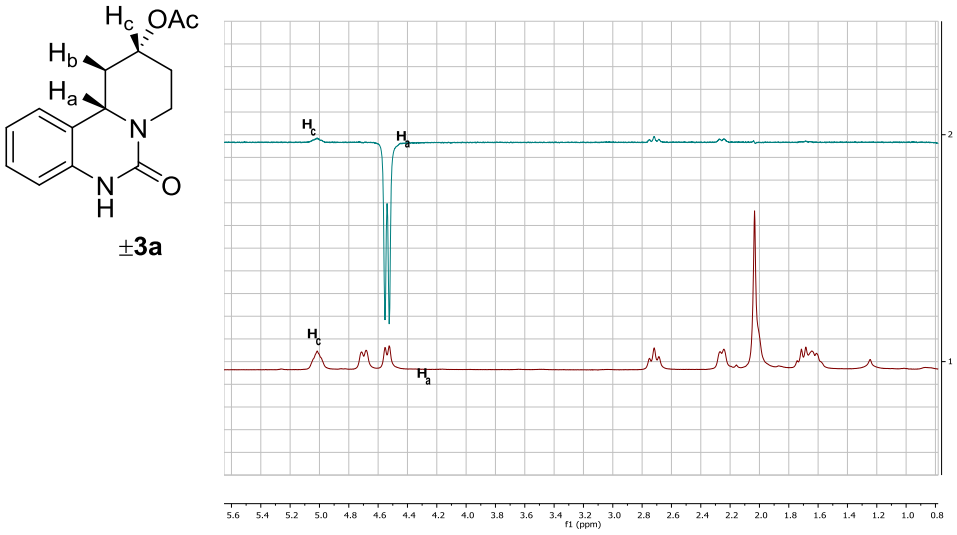
^{1}H NMR (400 MHz; $CDCl_3$) δ 1.17 (t, *J* = 7.1 Hz, 3H), 1.42–1.68 (m, 2H), 1.91 (ddd, *J* = 12.7, 4.8, 2.3 Hz, 1H), 1.96 (s, 3H), 2.12 (ddt, *J* = 12.4, 4.6, 2.3, 2.3 Hz, 1H), 2.65 (ddd, *J* = 13.8, 12.9, 2.6 Hz, 1H), 3.80 (dq, *J* = 14.5, 7.1, 7.1, 7.1 Hz, 1H), 3.94 (dd, *J* = 14.5, 7.2 Hz, 1H), 4.37 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.56 (ddd, *J* = 13.8, 4.6, 2.4 Hz, 1H), 4.94 (tt, *J* = 11.3, 11.3, 4.7, 4.7 Hz, 1H), 6.78 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.89 (td, *J* = 7.5, 7.4, 1.1 Hz, 1H), 6.98 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.14–7.18 (m, 1H).

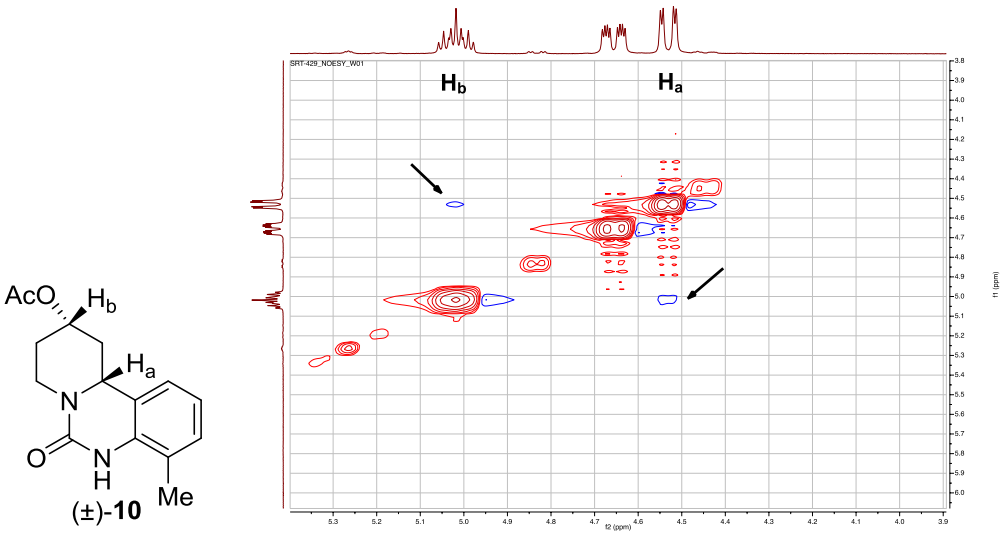
^{13}C NMR (100 MHz; $CDCl_3$) δ 12.7, 21.3, 30.2, 37.7, 39.2, 43.0, 55.9, 71.1, 112.9, 121.8, 121.8, 125.8, 128.5, 136.9, 152.8, 170.4.

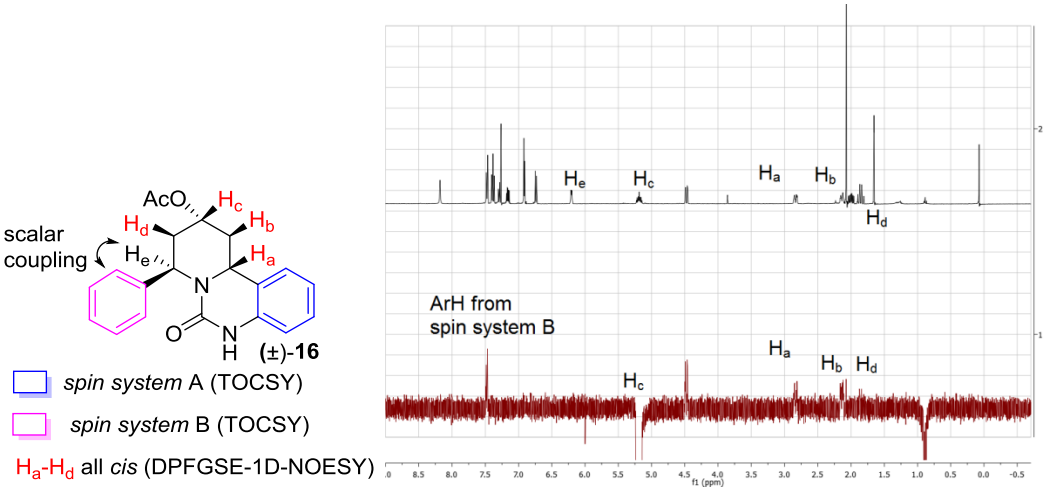
HRMS (ESI) calc'd for $C_{14}H_{16}N_3O_2$ *m/z* 258.1243, found *m/z* 258.1249 (MeCN + H^+ adduct).

NOE experiments for the determination of relative stereochemistry of compounds 3a, 10 and 16

The relative stereochemistry of aza-Prins compounds were determined by NOESY, DPGSE-1D-NOESY, COSY, TOCSY and X-ray diffraction studies (for compound **10**). For all compounds, a *cis* relationship exists between the benzylic hydrogen (H_a) and the hydrogen adjacent to the acetyl group (H_c). The introduction of a benzylic phenyl substituent did not have any effect on this relationship. Typically, NOE mixing times of 500–800 ms were used for selective irradiation experiments.







Literature references

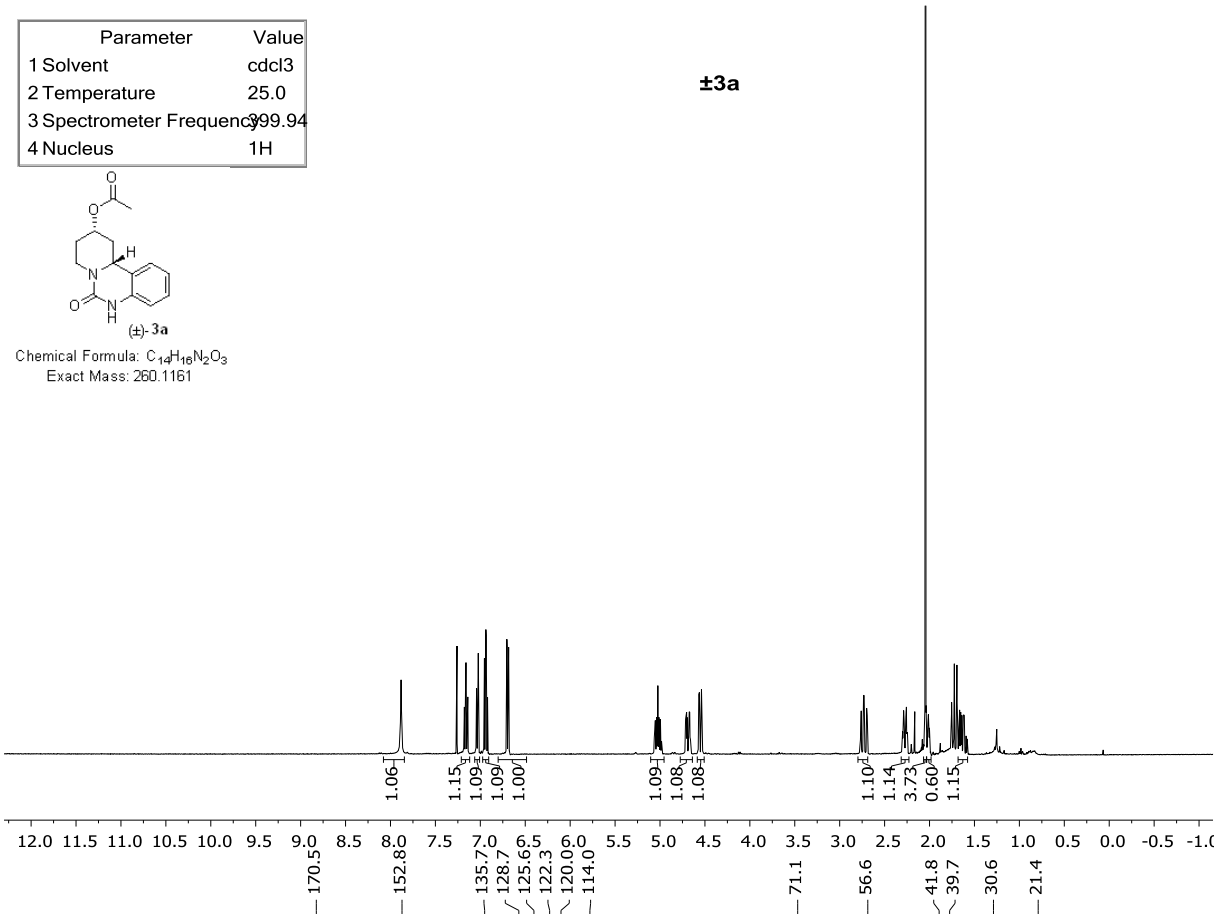
[1] M. Y. Stevens, K. Wieckowski, P. Wu, R. T. Sawant, L. R. Odell, *Organic & biomolecular chemistry* **2015**, *13*, 2044–2054.

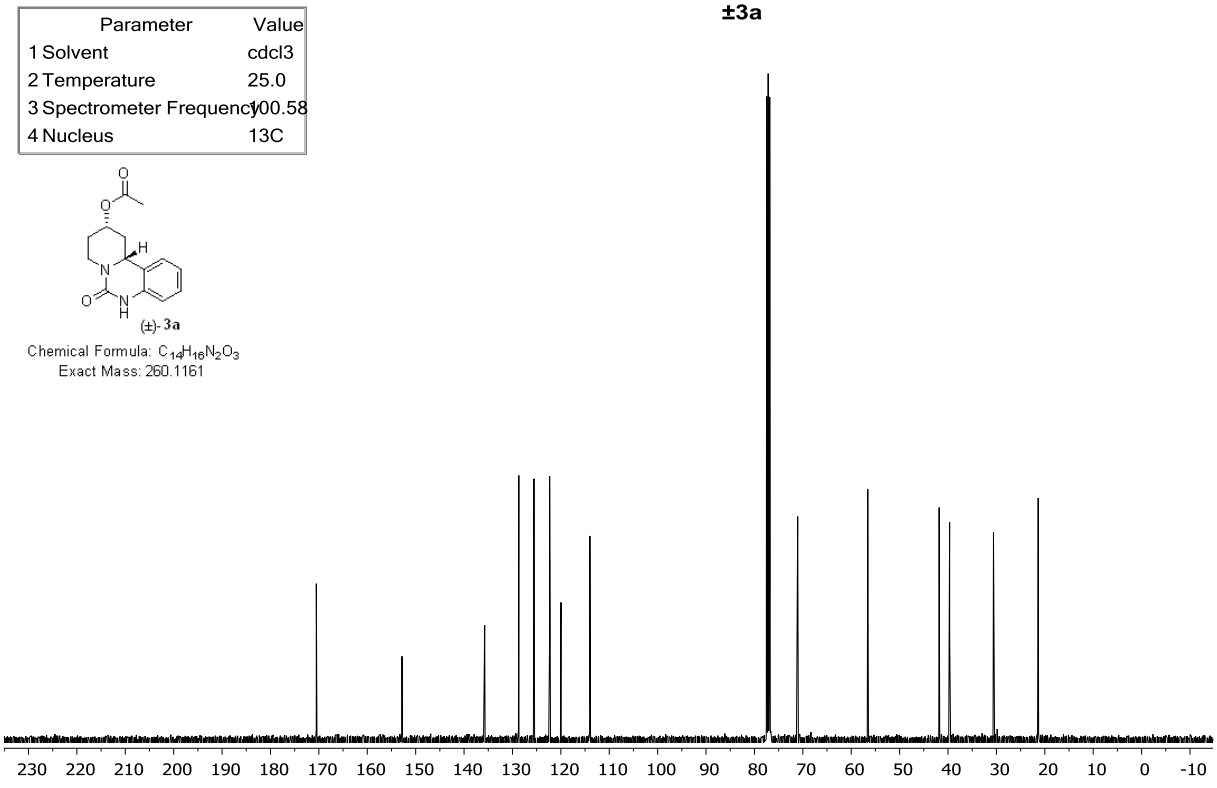
[2] R. T. Sawant, M. Y. Stevens, L. R. Odell, *European Journal of Organic Chemistry*

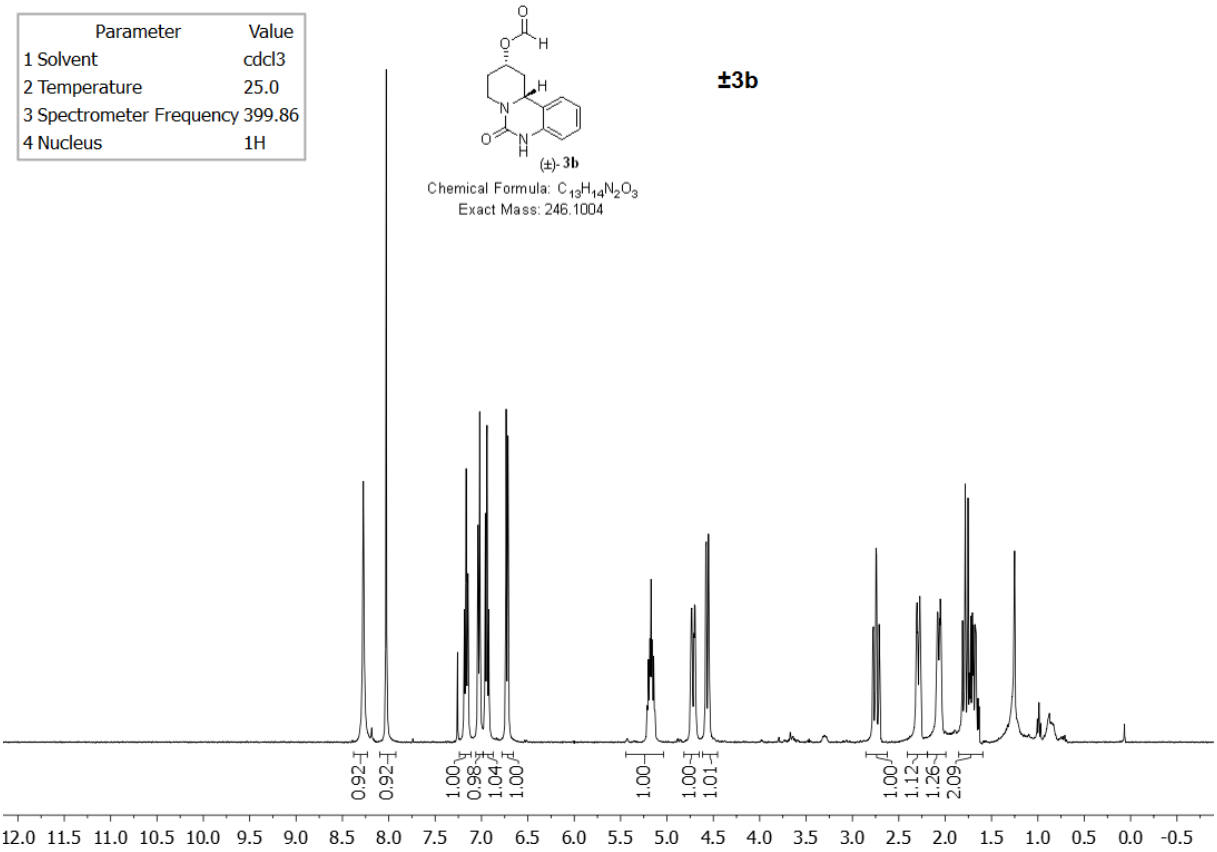
2015, *2015*, 7743–7755.

[3] S. Pramanik, R. R. Reddy, P. Ghorai, *Journal of Organic Chemistry* **2015**, *80*, 3656–3663.

^{1}H and ^{13}C NMR spectra



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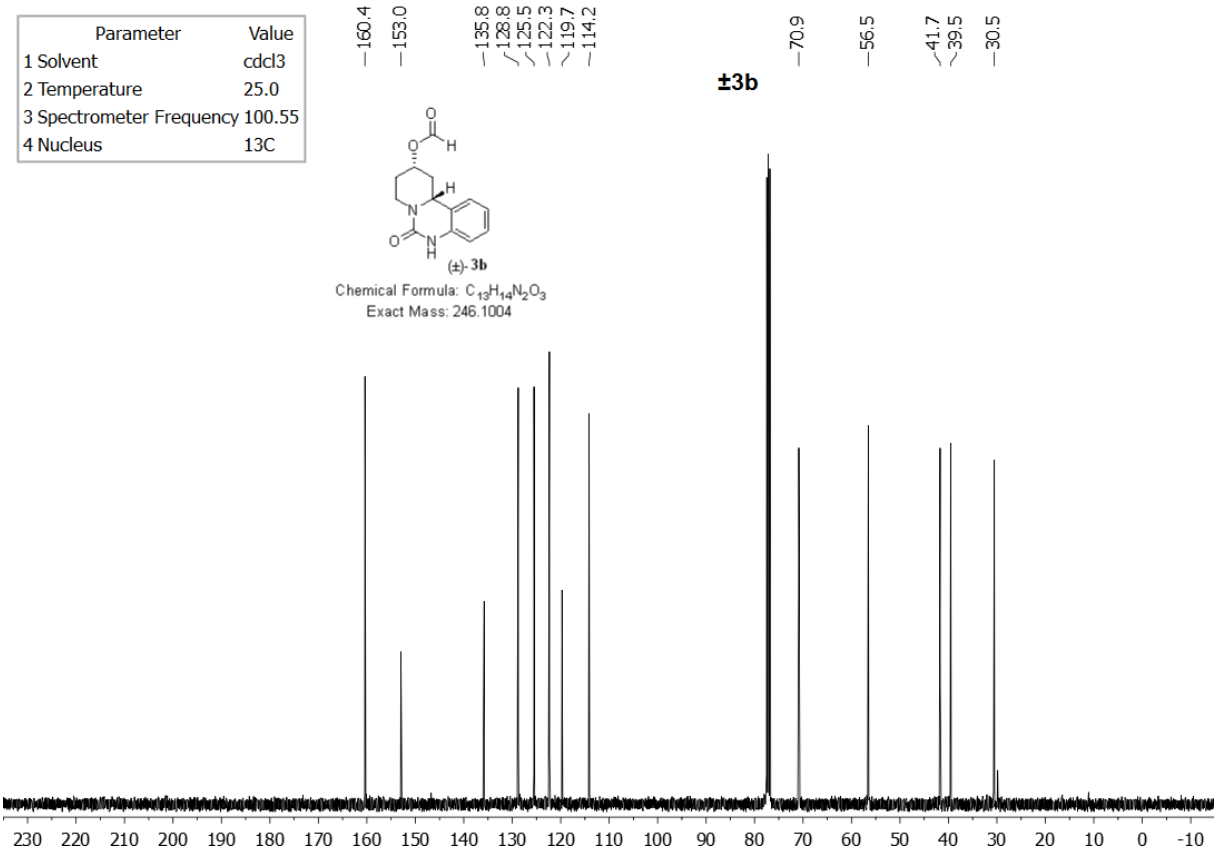
4 Nucleus 1H
±3b
(±)-3b
Chemical Formula: C13H14N2O3
Exact Mass: 246.1004
0.92 0.92 1.00 0.98 1.04 1.00 1.00 1.00 1.01 1.00 1.12 1.26 2.09
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5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±3b
(±)-3b
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Exact Mass: 246.1004
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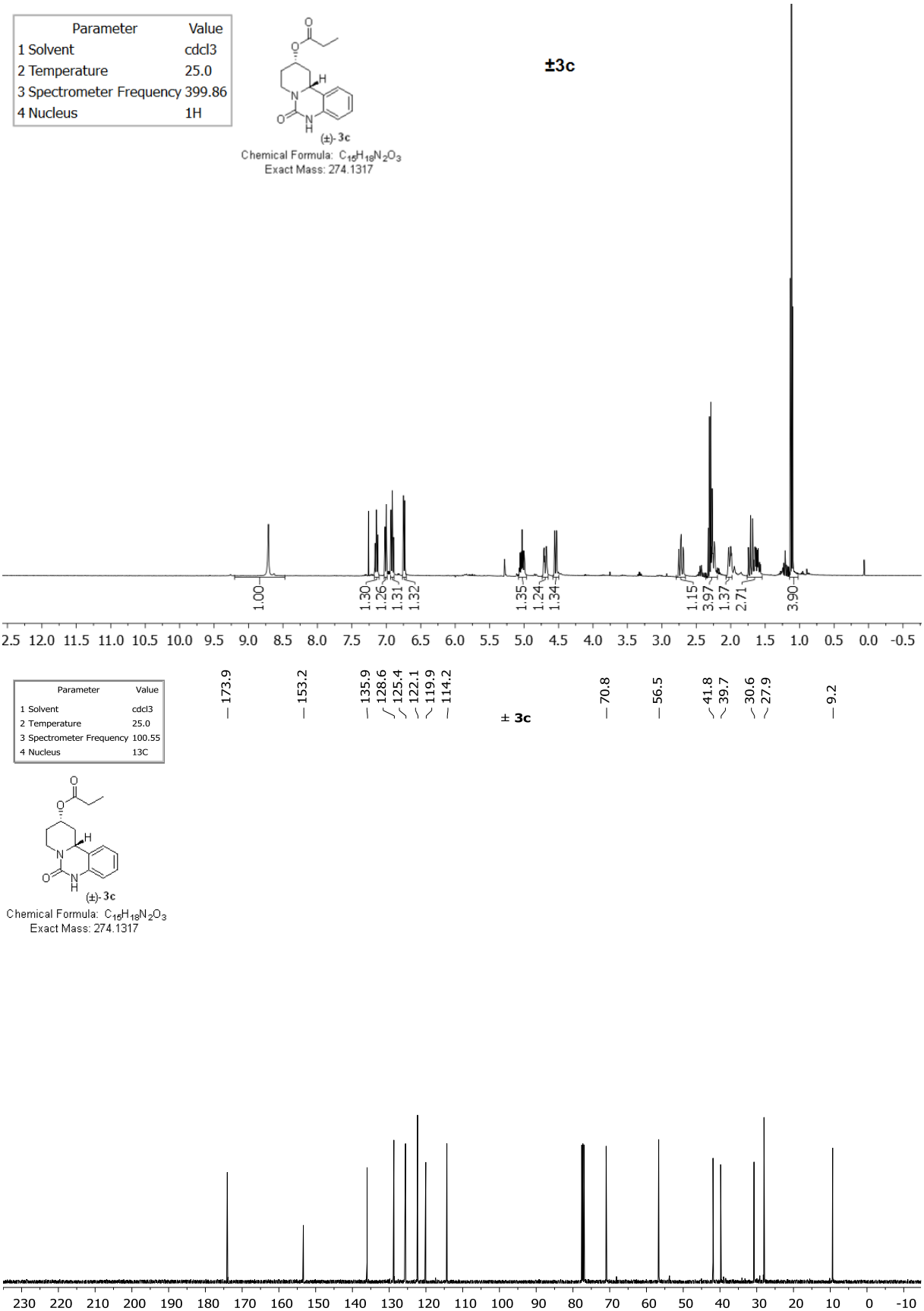
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2 Temperature 25.0
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4 Nucleus 1H
(±)-3c
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Exact Mass: 274.1317
±3c
1.00 1.30 1.26 1.31 1.32 1.35 1.24 1.34 1.15 3.97 1.37 2.71 3.90
2.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
Parameter Value
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3 Spectrometer Frequency 100.55
4 Nucleus 13C
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± 3c
(±)-3c
Chemical Formula: C15H18N2O3
Exact Mass: 274.1317
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

Parameter	Value
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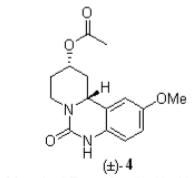
2 Temperature	25.0
3 Spectrometer Frequency	399.94
4 Nucleus	1H



(±)-**4**

Chemical Formula: $C_{15}H_{18}N_2O_4$

Exact Mass: 290.1267

±4

Parameter	Value
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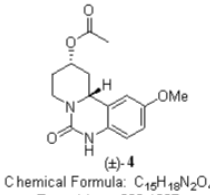
3 Spectrometer Frequency	100.58
4 Nucleus	13C

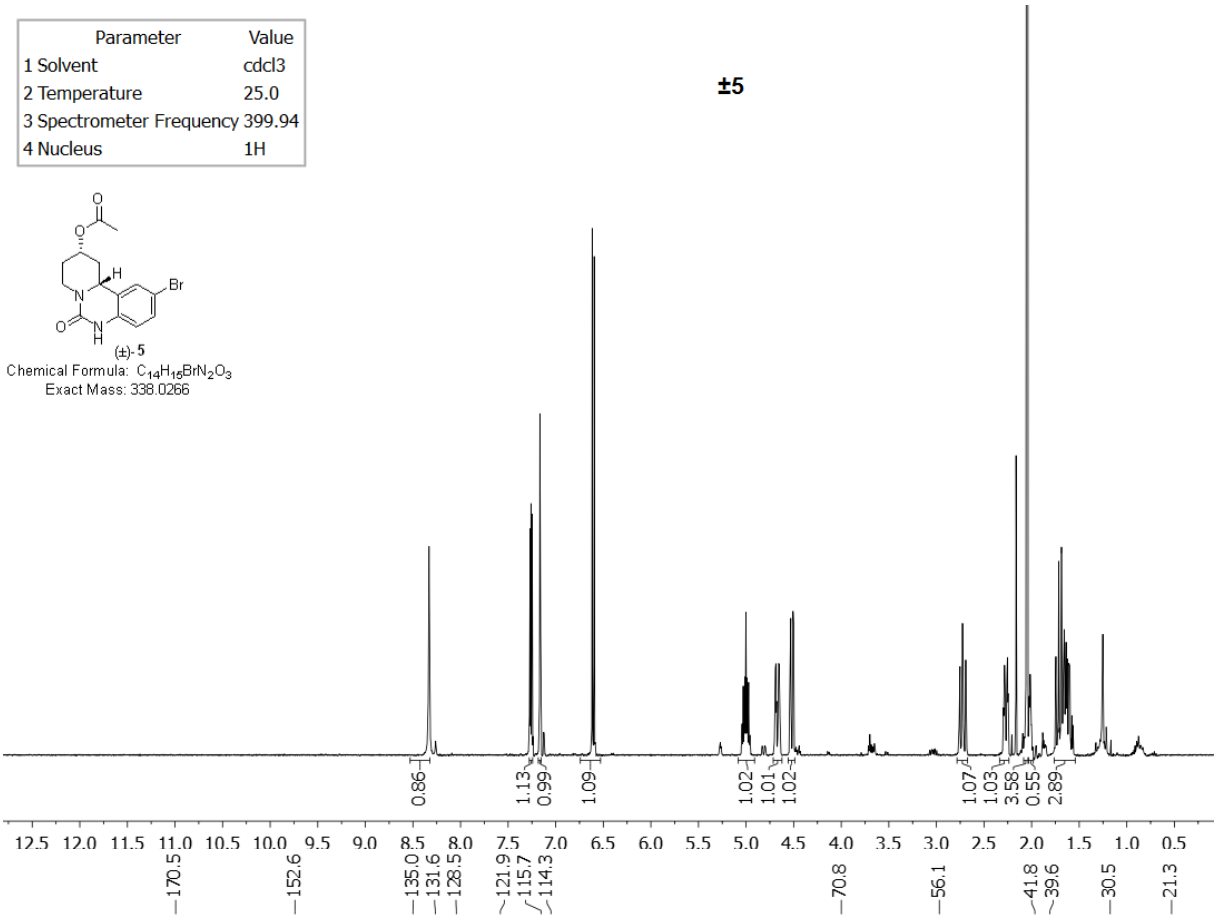


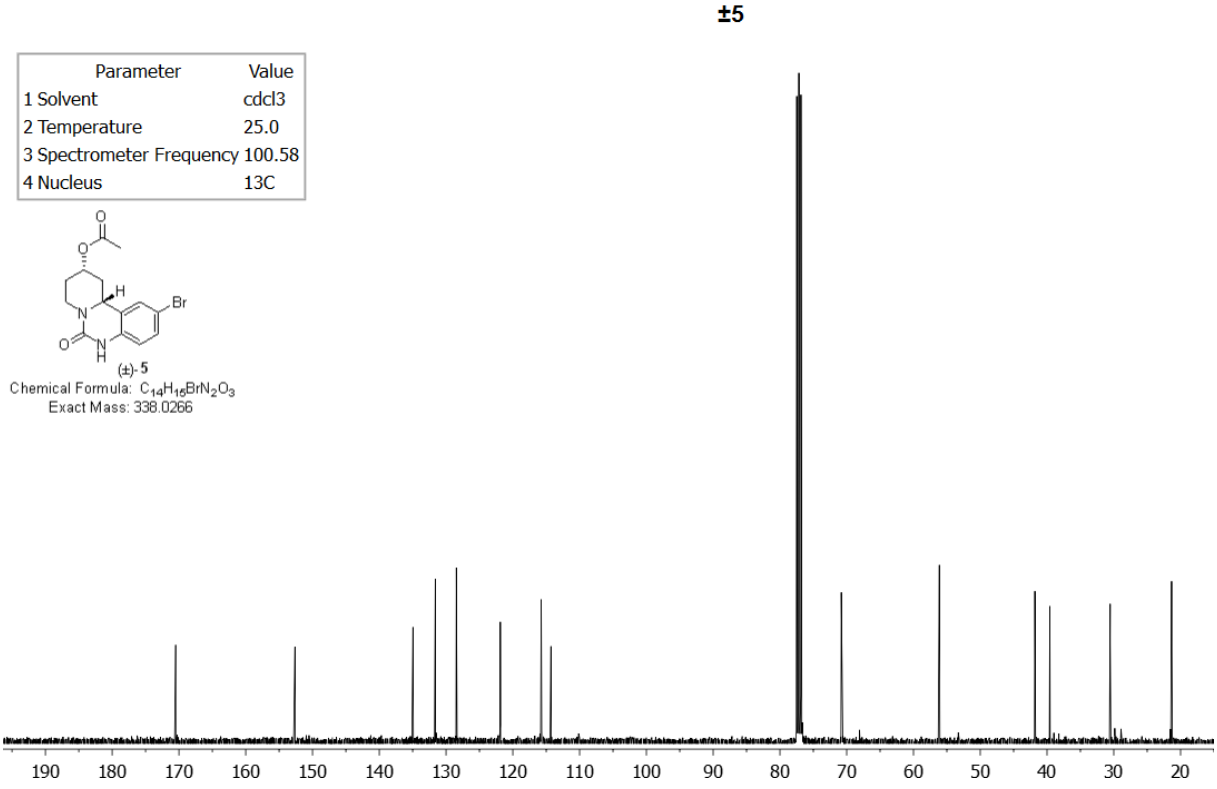
(±)-**4**

Chemical Formula: $C_{15}H_{18}N_2O_4$

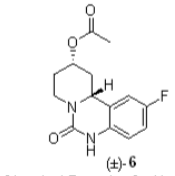
Exact Mass: 290.1267

±4


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 399.94
4 Nucleus 1H
±5
(±)-5
Chemical Formula: C14H16BrN2O3
Exact Mass: 338.0266
0.86
1.13
0.99
1.09
1.02
1.01
1.02
1.07
1.03
3.58
0.55
2.89
170.5
152.6
135.0
131.6
128.5
121.9
115.7
114.3
70.8
56.1
41.8
39.6
30.5
21.3


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 100.58
4 Nucleus 13C
±5
(±)-5
Chemical Formula: C14H16BrN2O3
Exact Mass: 338.0266

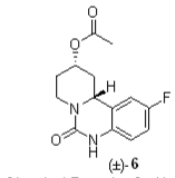
Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	399.86
4 Nucleus	1H



(±)-**6**
Chemical Formula: $C_{14}H_{15}FN_2O_3$
Exact Mass: 278.1067

±6

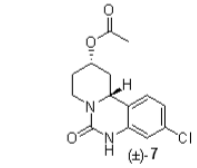
Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	100.55
4 Nucleus	13C



(±)-**6**
Chemical Formula: $C_{14}H_{15}FN_2O_3$
Exact Mass: 278.1067

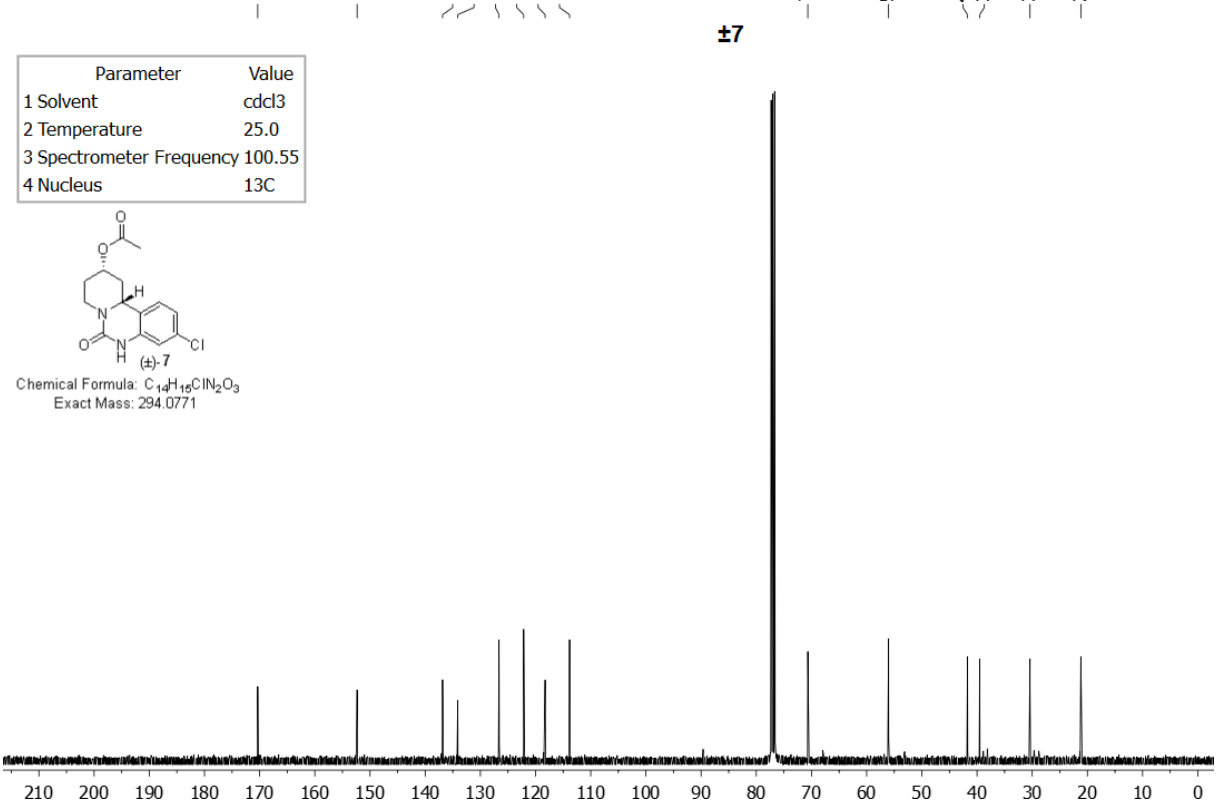
±6

Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	399.86
4 Nucleus	1H



(±)-7

Chemical Formula: $C_{14}H_{15}ClN_2O_3$
Exact Mass: 294.0771

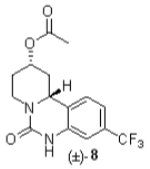


Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	100.55
4 Nucleus	13C

(±)-7

Chemical Formula: $C_{14}H_{15}ClN_2O_3$
Exact Mass: 294.0771

Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	399.86
4 Nucleus	1H

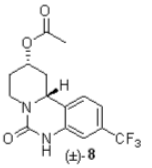


(±)-**8**

Chemical Formula: $C_{15}H_{15}F_3N_2O_3$
Exact Mass: 328.1035

±8

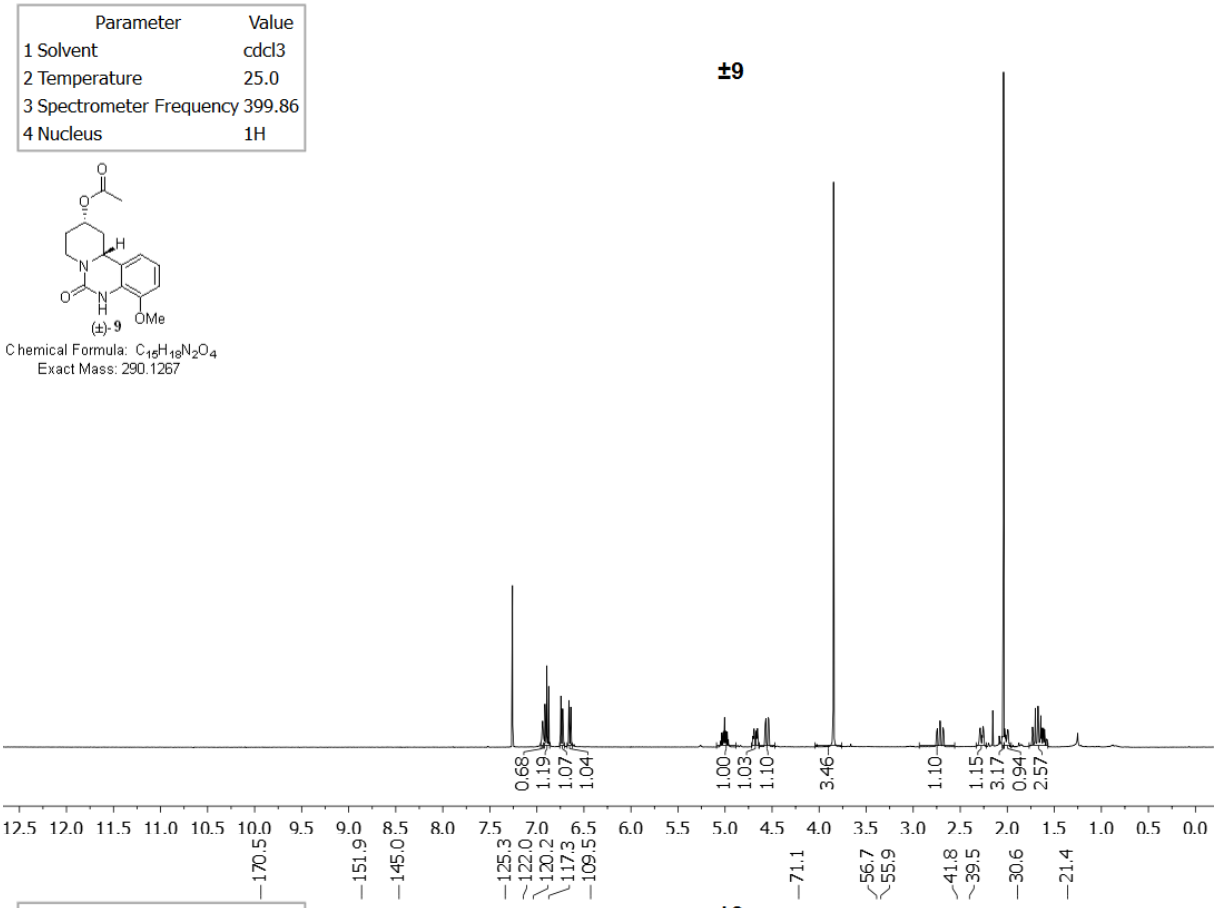
Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	100.55
4 Nucleus	13C

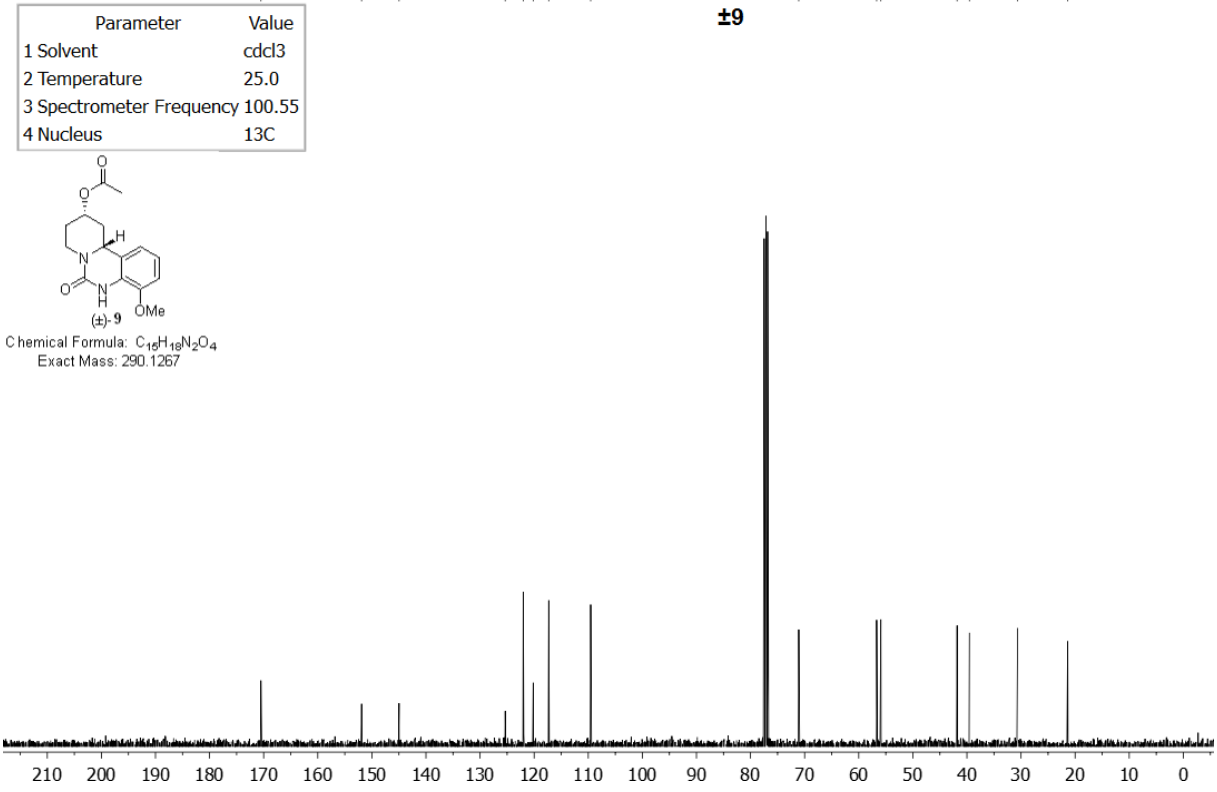


(±)-**8**

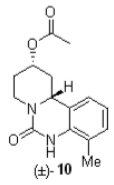
Chemical Formula: $C_{15}H_{15}F_3N_2O_3$
Exact Mass: 328.1035

±8


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 399.86
4 Nucleus 1H
±9
(±)-9
Chemical Formula: C15H18N2O4
Exact Mass: 290.1267
0.68 1.19 1.07 1.04 1.00 1.03 1.10 3.46 1.10 1.15 3.17 0.94 2.57
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 100.55
4 Nucleus 13C
±9
(±)-9
Chemical Formula: C15H18N2O4
Exact Mass: 290.1267
170.5 151.9 145.0 125.3 122.0 120.2 117.3 109.5 71.1 56.7 55.9 41.8 39.5 30.6 21.4
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

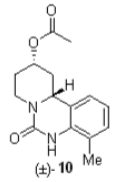
Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	399.86
4 Nucleus	1H



(±)- **10**

Chemical Formula: $C_{15}H_{18}N_2O_3$
Exact Mass: 274.1317

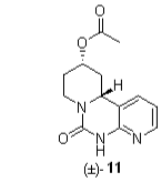
Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	100.55
4 Nucleus	13C



(±)- **10**

Chemical Formula: $C_{15}H_{18}N_2O_3$
Exact Mass: 274.1317

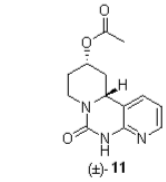
Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	399.86
4 Nucleus	1H



(±)-**11**

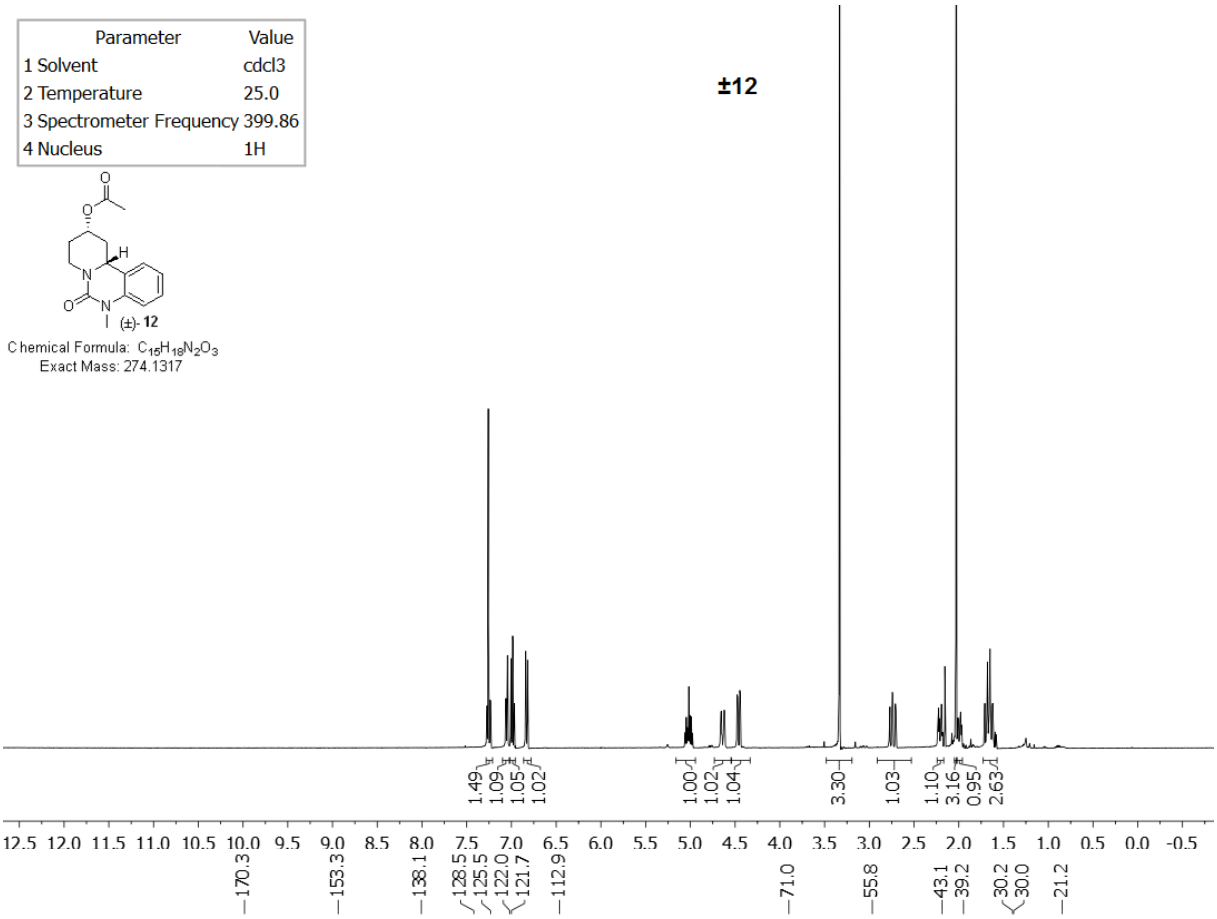
Chemical Formula: $C_{13}H_{15}N_3O_3$
Exact Mass: 261.1113

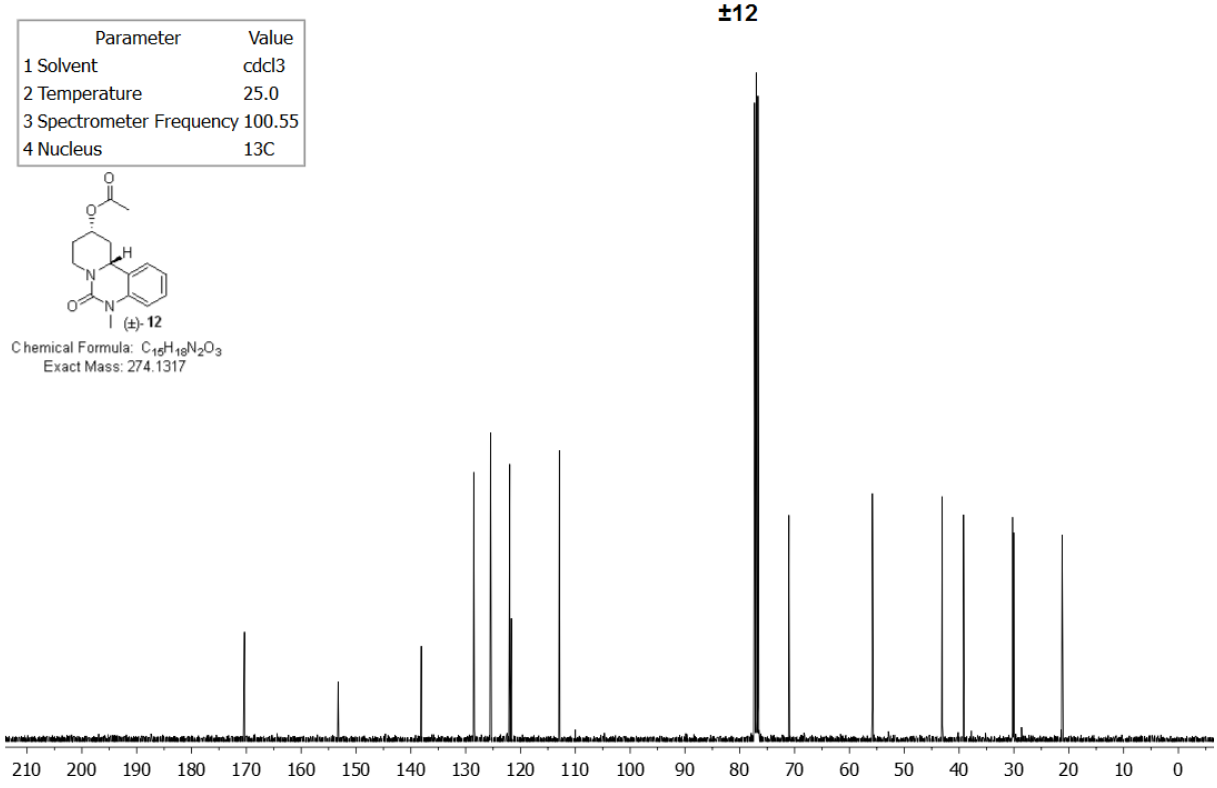
Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	100.55
4 Nucleus	13C



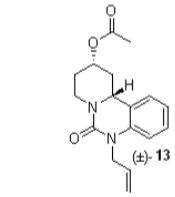
(±)-**11**

Chemical Formula: $C_{13}H_{15}N_3O_3$
Exact Mass: 261.1113


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 399.86
4 Nucleus 1H
±12
(±)-12
Chemical Formula: C15H18N2O3
Exact Mass: 274.1317
1.49 1.09 1.05 1.02 1.00 1.02 1.04 3.30 1.03 1.10 3.16 0.95 2.63
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 100.55
4 Nucleus 13C
±12
(±)-12
Chemical Formula: C15H18N2O3
Exact Mass: 274.1317
170.3 153.3 138.1 128.5 125.5 122.0 121.7 112.9 71.0 55.8 43.1 39.2 30.2 30.0 21.2
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	399.86
4 Nucleus	1H

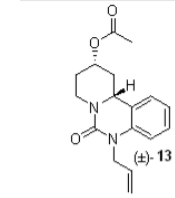


Chemical Formula: $C_{17}H_{20}N_2O_3$
Exact Mass: 300.1474

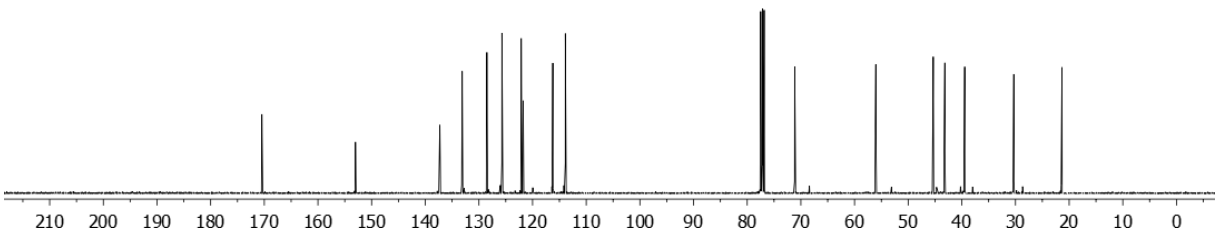
±13

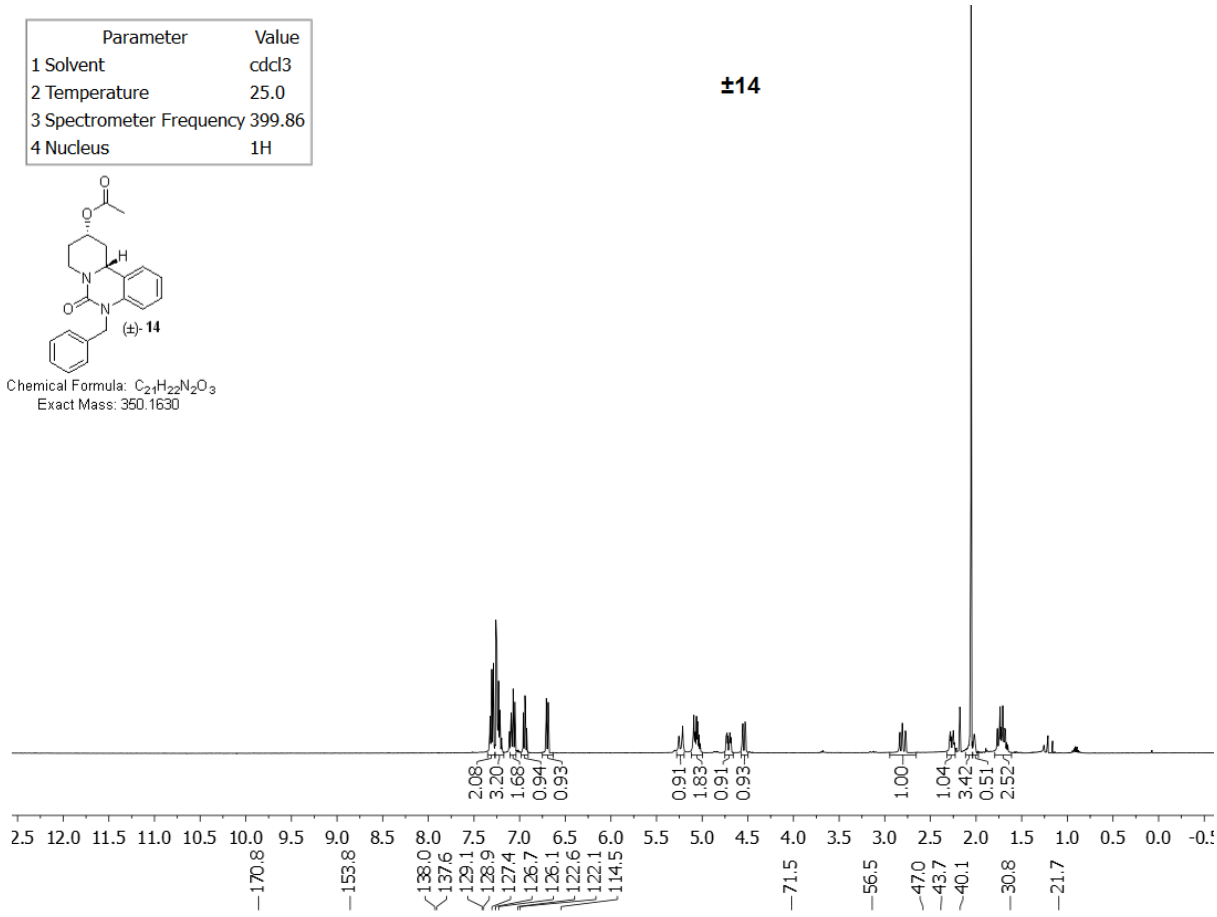
±13

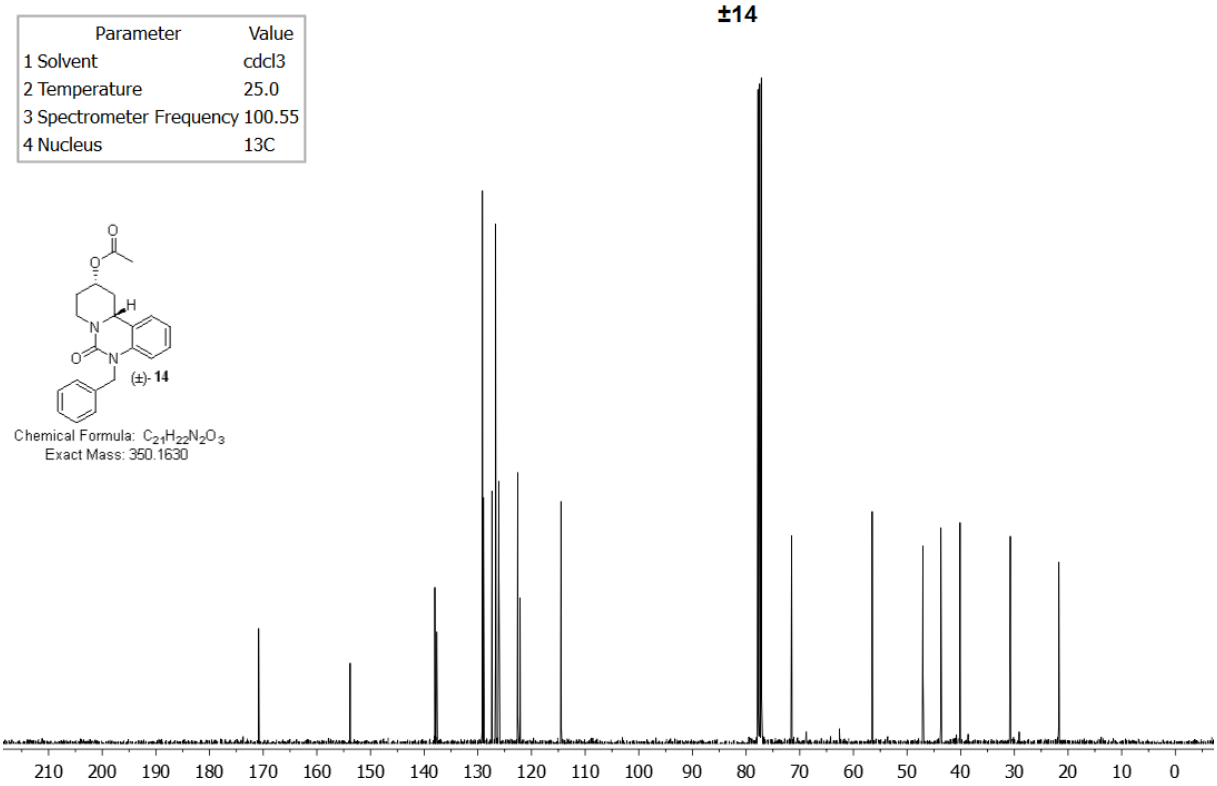
Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	100.55
4 Nucleus	13C

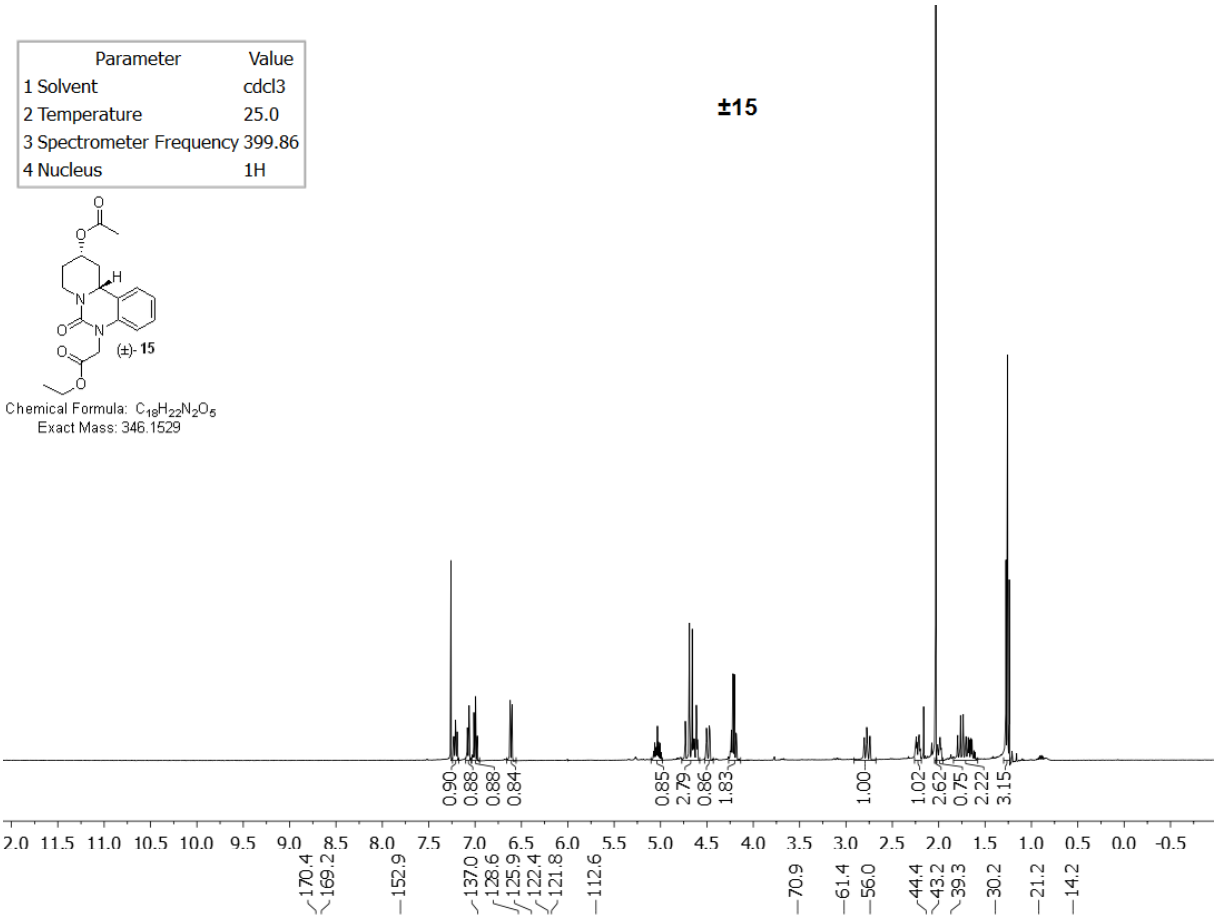


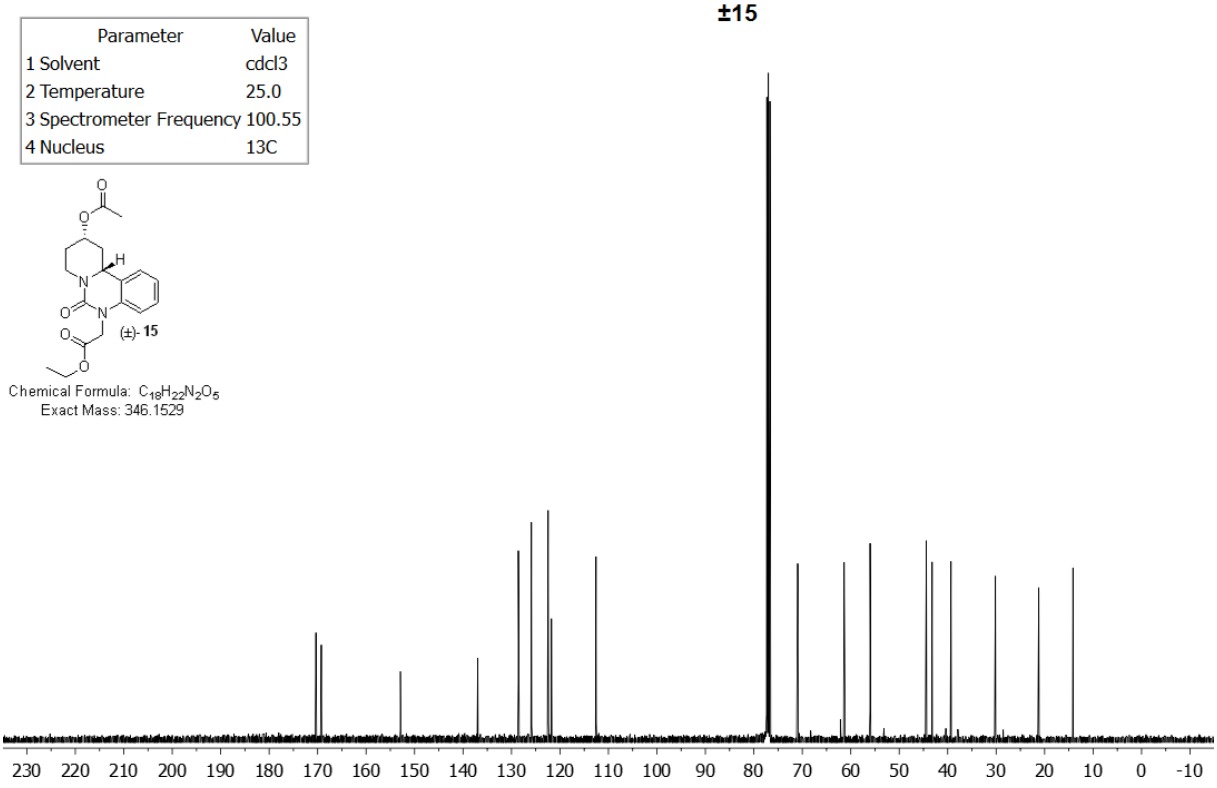
Chemical Formula: $C_{17}H_{20}N_2O_3$
Exact Mass: 300.1474

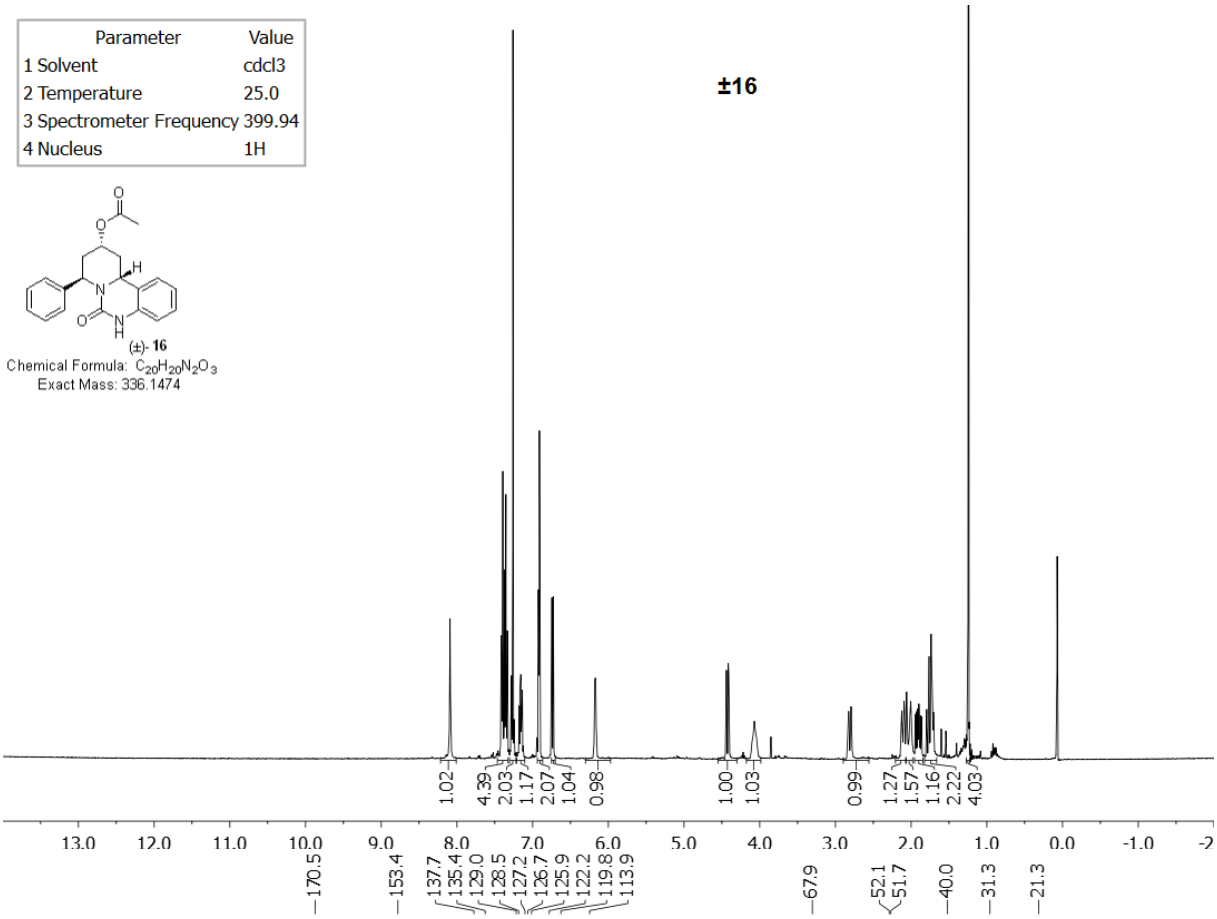


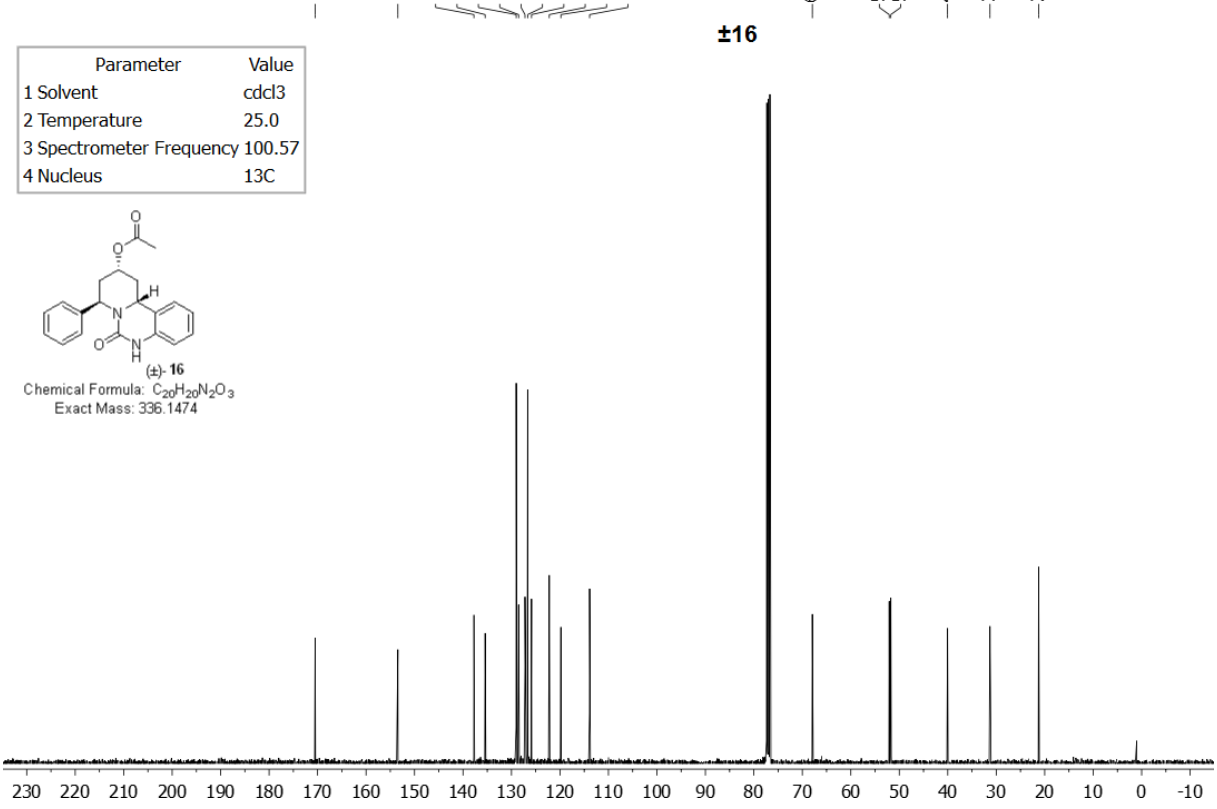

Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 399.86
4 Nucleus 1H
±14
(±)-14
Chemical Formula: C21H22N2O3
Exact Mass: 350.1630
2.08 3.20 1.68 0.94 0.93 0.91 1.83 0.91 0.93 1.00 1.04 3.42 0.51 2.52
170.8 153.8 138.0 137.6 129.1 128.9 127.4 126.7 126.1 122.6 122.1 114.5 71.5 56.5 47.0 43.7 40.1 30.8 21.7


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 100.55
4 Nucleus 13C
±14
(±)-14
Chemical Formula: C21H22N2O3
Exact Mass: 350.1630

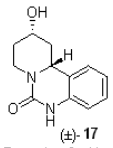

Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 399.86
4 Nucleus 1H
±15
(±)- 15
Chemical Formula: C18H22N2O5
Exact Mass: 346.1529
0.90 0.88 0.88 0.84 0.85 2.79 0.86 1.83 1.00 1.02 2.62 0.75 2.22 3.15
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 100.55
4 Nucleus 13C
±15
(±)- 15
Chemical Formula: C18H22N2O5
Exact Mass: 346.1529
170.4 169.2 152.9 137.0 128.6 125.9 122.4 121.8 112.6 70.9 61.4 56.0 44.4 43.2 39.3 30.2 21.2 14.2
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 399.94
4 Nucleus 1H
±16
(±)-16
Chemical Formula: C20H20N2O3
Exact Mass: 336.1474
1.02
4.39
2.03
1.17
2.07
1.04
0.98
1.00
1.03
0.99
1.27
1.57
1.16
2.22
4.03
13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0 -2
170.5
153.4
137.7
135.4
129.0
128.5
127.2
126.7
125.9
122.2
119.8
113.9
67.9
52.1
51.7
40.0
31.3
21.3


Parameter Value
1 Solvent cdcl3
2 Temperature 25.0
3 Spectrometer Frequency 100.57
4 Nucleus 13C
±16
(±)-16
Chemical Formula: C20H20N2O3
Exact Mass: 336.1474
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

Parameter	Value
1 Solvent	MeOD
2 Temperature	298.0
3 Spectrometer Frequency	400.13
4 Nucleus	1H

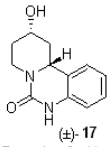


(±)-**17**

Chemical Formula: $C_{12}H_{14}N_2O_2$

Exact Mass: 218.1055

Parameter	Value
1 Solvent	CD3OD_SPE
2 Temperature	298.0
3 Spectrometer Frequency	100.62
4 Nucleus	13C

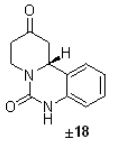


(±)-**17**

Chemical Formula: $C_{12}H_{14}N_2O_2$

Exact Mass: 218.1055

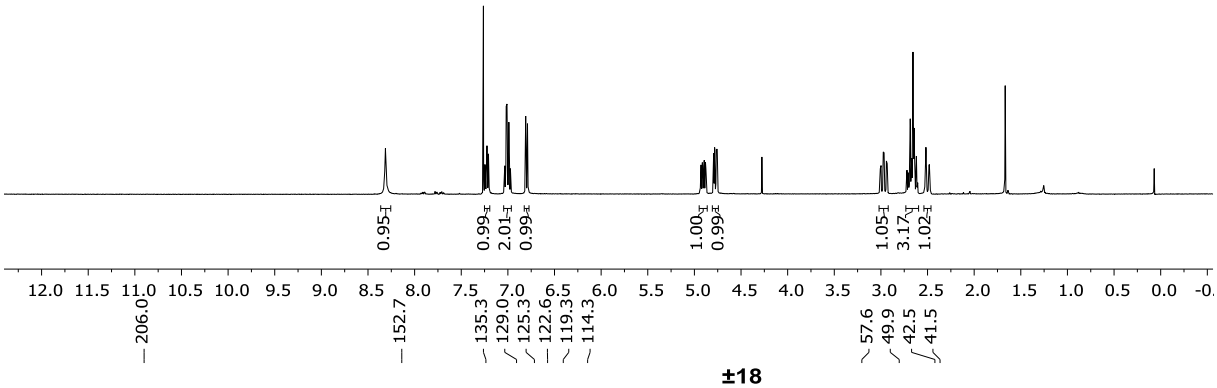
Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	399.86
4 Nucleus	1H



±18

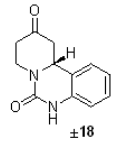
Chemical Formula: $C_{12}H_{12}N_2O_2$
Exact Mass: 216.0899

±18



±18

Parameter	Value
1 Solvent	cdcl3
2 Temperature	25.0
3 Spectrometer Frequency	100.55
4 Nucleus	13C

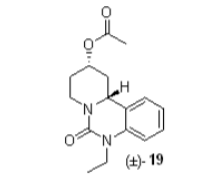


±18

Chemical Formula: $C_{12}H_{12}N_2O_2$
Exact Mass: 216.0899

Parameter	Value
1 Solvent	CDCl3
2 Temperature	298.0
3 Spectrometer Frequency	400.13
4 Nucleus	1H

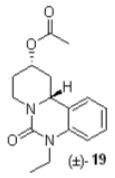
±19



Chemical Formula: $C_{16}H_{20}N_2O_3$
Exact Mass: 288.1474

±19

Parameter	Value
1 Solvent	CDCl3
2 Temperature	298.0
3 Spectrometer Frequency	100.62
4 Nucleus	13C



Chemical Formula: $C_{16}H_{20}N_2O_3$
Exact Mass: 288.1474